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Whitepaper

A GLOBAL INDUSTRY AND MARKET RESEARCH REPORT ON INJECTION SITE REACTIONS

Highlighting how SCARLETRED Enables Remote ISR Monitoring and Objective Quantification

Including an Implementation Guide for Biopharma, Cosmetics, and Telemedicine

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V1.0

scarletred

SCARLETRED is a Vienna- and Boston-based digital health company revolutionising the global dermatology and telemedicine market. Our first product is the multi-award winning Scarletred® Vision software platform, a CE certified mobile medical device powered by a proprietary artificial intelligence core. It is the first technology in the world which enables objective skin imaging and remote skin analysis in more than 3000 cutaneous disorders. With the start of the coronavirus pandemic in 2020 Scarletred® Vision gained a big momentum in vaccination industry who quickly adopted the new technology for safety monitoring of Covid-19 injections. The company roled out also the novel eCOVID19 telemedicine platform to elderly care homes and drug stores for home based health monitoring. SCARLETRED is ISO13485 certified and honored with the Austria State Prize Digital Solution.

GDPR

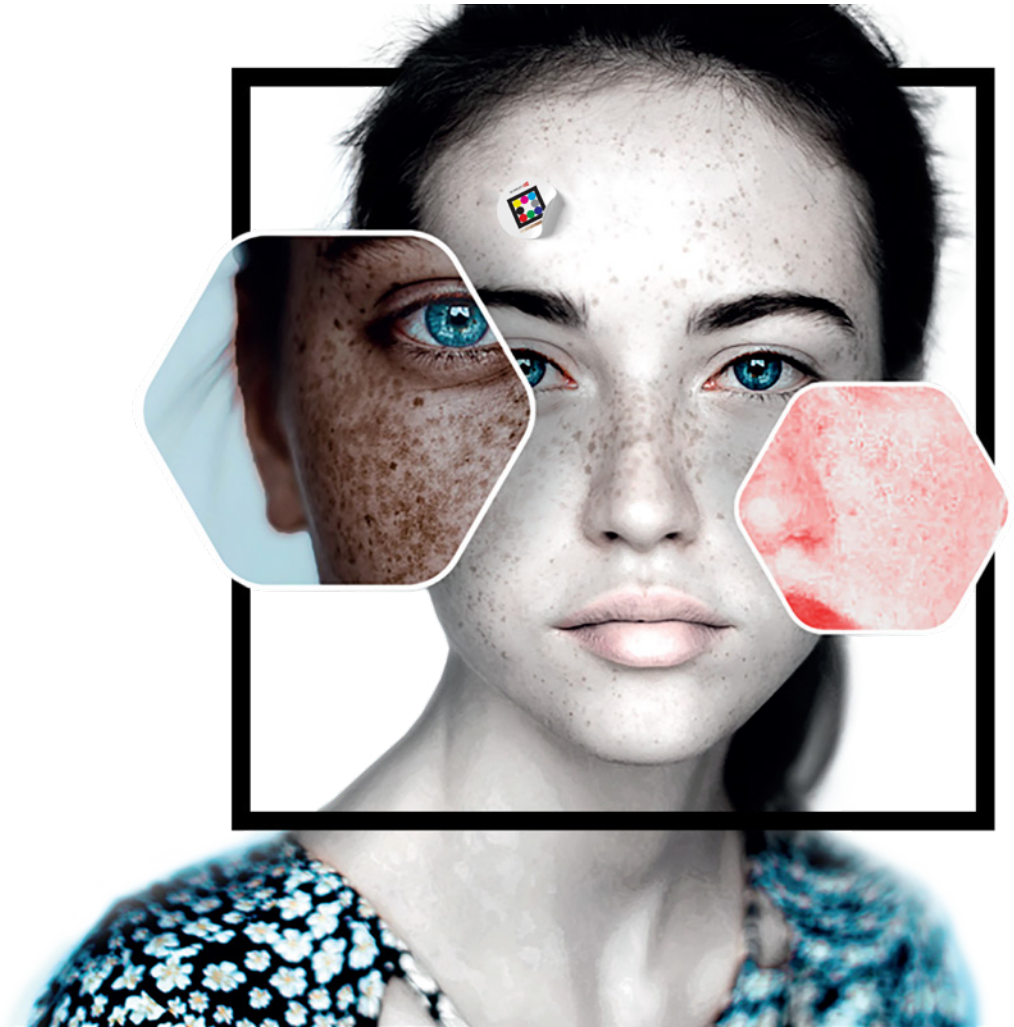
MEDICAL DEVICE ISO 13485

CE Class I

HIPAA COMPLIANT

INTELLECTUAL PATENTED PROPERTY

ICH GCP 100% COMPLIANT



Abstract

Injection site reactions (ISRs) are a constellation of symptoms, such as erythema, swelling, pain, and induration, occurring at the site of the injection. Documenting and monitoring ISRs are integral components of the clinical trial process for any injectable drug or treatment. During clinical development, local reactions at the injection site must be tracked to complete the safety assessment of the investigational product. ISRs can occur right after the substance has been administered and subsequently evolve over time after the individual has left the health care provider, highlighting the need for a solution that can accommodate real-time, remote, home-based monitoring. Medical professionals agree that traditional methods of ISR monitoring in the product development phases are lacking, leading to a loss of time, precision, and data. The global digitalization trend and the impact of the current SARS-CoV-2 pandemic are the main driving forces behind the development of new injectables, revealing the urgent requirement for novel state-of-the-art tools that can be more efficiently implemented. In the present global market and research study, we (SCARLETRED) give an overview of the applicable industries and our technological solution, Scarletred®Vision, which outperforms conventional methods and is on its way to becoming the modern standard for remote ISR Monitoring and objective quantification in a broad range of application fields.

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Keywords

Injection site reaction, pharmaceuticals, pharma, cosmeceuticals, cosmetic industry, vaccinations, immunotherapeutics, chemotherapy, oncology, chemotherapeutics, immunotherapy, remote home-based monitoring, telemedicine, telehealth, teledermatology, clinical trials, virtual clinical trials, oligonucleotide therapy,

INTRODUCTION

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INJECTION SITE REACTIONS

An injection site reaction (ISR) refers to a range of symptoms that can occur at the site of injection after a drug or treatment has been administered. Such reactions emerge from using a wide range of injectables relevant to intravenous, intramuscular, intraarticular, and subcutaneous injections. ISRs typically manifest as erythema, itchiness, pain, swelling or bruising, rash, or bleeding [1]. Although these reactions are frequently mild and self-limiting, generally only requiring simple treatment and subsiding in approximately 3-5 days, their documentation is still required. On the other hand, some ISRs can be more severe and include significant local reactions which extend from one joint to another or may emerge as ulceration or necrosis [2].

ISRs occur in response to the excipient or the product itself (drug, cosmetics, and others) and are divided into two groups: irritation reactions and allergic reactions. Irritation reactions are generally immediate or appear shortly after injection due to sensitivity to the injected substance. Allergic reactions happen especially during hyposensitization. Other reactions are extravasation reactions common with highly corrosive drugs (e.g. chemotherapeutics) which can subsequently leak from the blood vessels. Such reactions can be immediate or delayed and include the aforementioned manifestations of ISRs, yet can also extend to severe tissue damage, acute pain, and blistering [3].

Documenting and monitoring ISRs are of great importance for the safety assessment of novel investigational therapeutic products in various applications, vaccine development, cancer therapies, cosmetic industry, and multiple biopharmaceuticals, each dealing with various forms of injectables. Doctors, clinicians, and healthcare practitioners experience ISR tracking as routine work and clinical trial procedures. The remote monitoring of ISRs is increasingly required to track patients' symptoms and clinical trial participants from home. As affected industries grow and the volume of developed products expands, professionals have become aware of the challenges involved in the implemented methods of ISR assessment, opening a window for modern digital and clinically validated medical device solutions.

LIMITATIONS OF CONVENTIONAL METHODS OF ASSESSMENT

Assessment of ISRs is essential to establish the safety and identify possible side effects of the injection itself, not to be confused with the safety of the investigational product. Conventional assessment methods include visual examinations, the use of rulers for scaling purposes, color charts, and other analog devices [Table 1]. While these traditional methods are accepted by the medical community owing to a lack of awareness of a better solution, their limitations include subjectivity, difficulty in quantifying ISRs, and inability to standardize procedures, for instance, within a hospital, let alone on a larger scale as is the case in multi-centric international clinical trials. Accordingly, industry leaders and experts agree that there is a pressing need for streamlining ISR tracking, particularly in clinical trial settings. Drugs and treatments produce starkly differing rates of ISRs, and the probability of these reactions depends on a multitude of factors. Consequently, each new product must be monitored closely over a period of time in order

	SCARLETRED®VISION	VISUAL EXAMINATION	COLOUR CHARTS	ANALOGUE DEVICES	QUESTIONNAIRE
ASSESSMENT OF AFFECTED VISIBLE AREA	✓	✓	X	✓	X
ASSESSMENT OF ERYTHEMA	✓	✓	✓	X	X
ASSESSMENT OF SWELLING AND PAIN	✓	X	X	X	X
DOCUMENTATION OF PAIN BY DESCRIPTION AT THE AFFECTED VISIBLE AREA	✓	X	X	X	✓
DOCUMENTATION OF INDURATION BY DESCRIPTION AT THE AFFECTED VISIBLE AREA	✓	✓	X	X	✓
STANDARDIZED HIGHT-QUALITY IMAGING	✓	X	X	X	X
OBJECTIVE DOCUMENTATION AND MEASUREMENT OF VISIBLE CHANGES	✓	X	X	X	X
SCORING OF VISIBLE SKIN CHANGES	✓	✓	X	✓	X

Table 1. Applications of Scarletred®Vision and other ISR monitoring methods.

to perform an accurate assessment. Currently, the needs of healthcare systems worldwide are shifting, and the market for various injectables continues to expand drastically. As the demands placed on research teams increase, the limitations of traditional methods for ISR documentation and monitoring become increasingly evident. Professionals recognize the following main challenges in the current landscape:

- ISRs are not tracked nearly enough during clinical trials; if they are monitored, then usually in case of severe worsening reactions or other complications and not at the onset of the ISR
- Image quality varies significantly between experts, and the ISRs are typically not quantified
- Lack of objectivity and inability to deliver a standardized method of assessment when used among different investigators
- Extensive amounts of time and effort are required for traditional methods of assessment, resulting in reproducibility and scalability issues
- Conventional visual assessment of erythema and changes to the skin does not allow for data to be quantified or shared in a reproducible way
- While specialized imaging machines can produce high-quality scans, they tend to be large, bulky, and expensive, excluding them from use in clinical trials due to scalability issues

The consensus within the medical community in both the pharmaceutical and cosmetic industries is clear: a strong need for a precise, scalable, easy to implement, and cost-efficient solution to document and monitor ISRs. To circumvent these limitations, an innovative digital and scalable solution is urgently needed. The substantial growth and product development underway in applicable industries highlights the magnitude of the challenges reported.

APPLICABLE INDUSTRIES

APPLICABLE INDUSTRIES

PHARMACEUTICALS

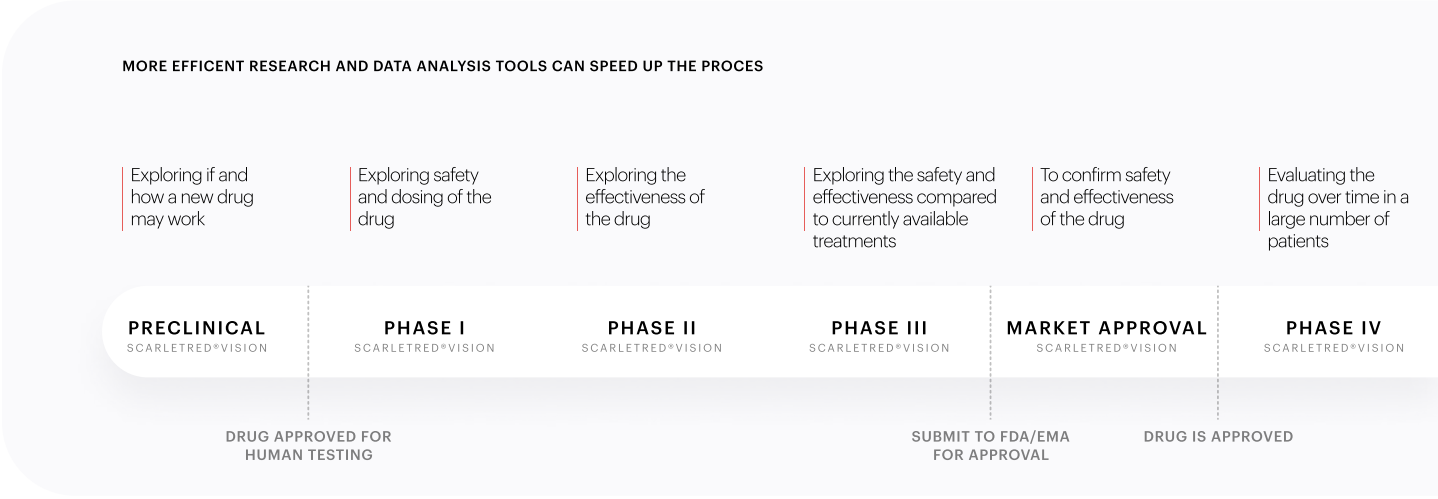


Figure 1. Clinical testing of pharmaceuticals; the use of more effective research and data analysis tools can speed up the process.

Vaccines

Vaccine Development and ISRs

After in-vitro testing phases have been completed, vaccines are tested on animals and subsequently on humans [Figure 1]. In the preclinical phase, although testing on animals, such as mice, may involve fewer regulatory hurdles and is an easier and safer endeavor to undertake, gathering as much data to ensure adequate documentation of any symptoms is of high value.

The same is applicable for the following phases of vaccine development, the human clinical trials. Regulatory bodies demand specific reporting of any adverse events at the site of vaccination. Injection site pain and erythema have been noted as the most commonly reported side effects after vaccine administration [4].

In the clinical trial setting, a great number of assessments must be made to characterize and classify ISRs. Professionals in the field concur that the time and effort required for traditional assessment methods are not suited to the demands of the process and do not necessarily yield the desired results, rendering the process obsolete. Even within the one multi-centric clinical trial, the acknowledged lack of objectivity and standardization makes the need for a new solution even more evident.

Global Vaccine Market

The first recorded vaccine was introduced by Edward Jenner against smallpox. Since then, scientific strides have opened the doors for vaccines to be used globally to prevent morbidity and mortality from a long list of infectious diseases. The global vaccine market was USD 46.88 billion in 2019 and is projected to reach USD 104.87 billion by 2027 [5]. Whole pathogen, sub-unit, and

combined vaccine types are accompanied by the rising popularity of nucleic acid vaccines, which appear to be promising for inducing immunity against HIV, Ebola, and SARS. Despite traditional vaccines' long-standing success, viral diseases that require new vaccines are understood to be more complex in their pathogenesis than previous ones. Thus, new approaches aimed at enhancing adaptive immunity of the immune system and focused on adjuvants, T-cell epitope mapping, and structure-based vaccine design are shaping the future of vaccine development [6]. Recent findings suggest that traditional vaccines drive the global market volume, while innovative vaccines drive the global market value clearly illustrate these dynamics.

The majority of the global population receives multiple vaccinations during their lifetimes. The following tables show the percentage of people receiving the different vaccines out of the eligible group for that treatment [Table 2].

The current COVID-19 outbreak has prompted the global market industry to develop a fast and effective solution while pointing out the healthcare systems' weak spots. As a result of consistent focus from government agencies worldwide and the efforts of several vaccine manufacturers, the global COVID-19 vaccine market size alone is expected to reach over USD 5 billion by 2024. New development strategies such as the combination of phase I and II clinical trials in addition to faster regulatory approval will pave the way for the increasing availability of COVID-19 vaccines globally [7]. This outbreak prompts manufacturers to focus on the fast-tracked clinical development of effective and safe vaccines and increase production capacities. The European Medicines Agency (EMA), Europe's equivalent to the U.S. Food and Drug Administration (FDA), plays a crucial role in enabling the development, evaluation, approval, and monitoring of COVID-19 vaccines within the EU, ensuring that they conform to safety and efficacy standards [8].

	REGION OF THE AMERICAS		EUROPEAN REGION	
BCG TUBERCULOSIS	83 2019	96 2015	92 2019	90 2015
DTP 1 TETANUS AND DIPHTHERIA TOXOIDS	90 2019	97 2015	97 2019	96 2015
DTP 3 TETANUS AND DIPHTHERIA TOXOIDS	84 2019	91 2015	95 2019	93 2015
HepB_BD HEPATITIS B	55 2019	54 2015	41 2019	41 2015
HepB3 HEPATITIS B	81 2019	89 2015	92 2019	82 2015
Hip3 HEMOFILIUS INFLUENCE	85 2019	91 2015	79 2019	76 2015
IPV1 INFANTILE PARALYSIS	86 2019	62 2015	95 2019	69 2015
MCV1 MENINGITIS	88 2019	93 2015	96 2019	94 2015
MCV2 MENINGITIS	75 2019	78 2015	92 2019	89 2015
PCV3 PNEUMOCOCCAL DISEASES	83 2019	85 2015	80 2019	48 2015
Pol3 POLIO	87 2019	92 2015	95 2019	94 2015
RCV1 RUBELLA	88 2019	93 2015	96 2019	94 2015
Rotac ROTAVIRUS	74 2019	76 2015	25 2019	23 2015
TT2plus TETANUS TOXOID	40 2019	48 2015	83 2019	83 2015
YFV YELLOW FEVER	60 2019	55 2015	- 2019	- 2015

Table 2: Comparison of the rate of vaccinations: Between 2015 and 2019, the Americas showed an overall decrease in vaccinations whilst the percentage of the European region population showed an increasing vaccination trend for that same period.

As of the beginning of Q2 2021, 89 vaccines are being tested in clinical trials on humans, with 23 having already reached the final testing stages. At least 77 preclinical vaccines are under active investigation [9].

Modern Challenges of Vaccine Development

Given the global pandemic, clinical trials for COVID-19 vaccines are currently required to be fast-tracked, ensuring the delivery of quality results in record time by compressing the standard development time of 10 - 15 years into a matter of months [Figure 1]. These events have drastically impacted the vaccine development industry, leading to faster adoption of novel state-of-the-art methods. The positive impact of the digital transformation of these processes is likely to go beyond the pandemic since they have shown that a concerted effort can lead to record-breaking clinical development timelines. Given the global urgency, safety and precise monitoring of these sped-up clinical trials are more relevant than ever [Figure 3].

Experts state that at least 70% of the world's population must be vaccinated to reach herd immunity and stop the SARS-CoV-2 virus from spreading, however, with the new variants emerging, herd immunity is expected to be closer to 84% [10]. If only 1% of vaccinated patients develop ISRs, 55 million people worldwide would need to be monitored to categorize a particular ISR [Figure 2]. Given the usually high percentage of ISRs related to vaccines, this is a conservative estimation. The urgency of the current situation magnifies the necessity for effective methods of streamlining the clinical trial and post-marketing surveillance processes.

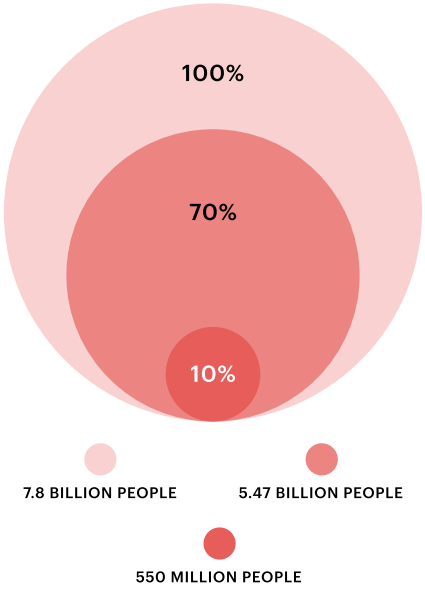


Figure 2. If only 1% of vaccinated patients develop ISrs, 550 million people worldwide would need to be monitored to categorize a particular ISR (SCARLETRED WSA Market Research 2021, Unpublished).

"Scarletred's solution-oriented team quickly realized that their technology can have a major impact in fighting the global pandemic. The ISR application is the company's latest use case in its feat to further revolutionize dermatology through groundbreaking digital technology. Today, the novel application is already being used in multiple COVID-19 vaccine studies across the US, Europe, and Asia, helping making vaccines safer for everyone."

Daniel Moertl
Technology and Innovation Officer
Austrian Trade Commission, New York

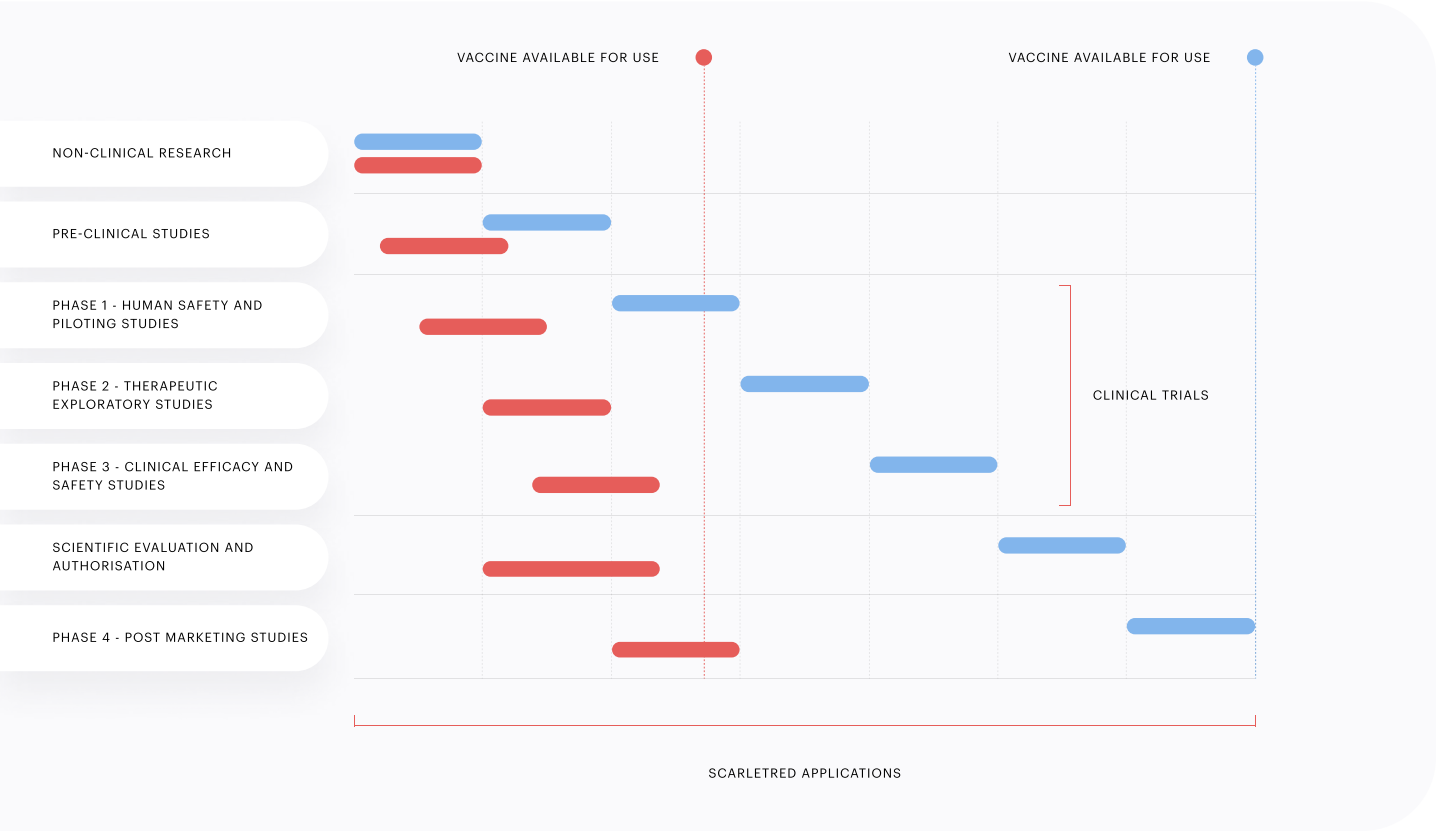


Figure 3. Standard timeline for vaccine development (blue) and the timeline for developing SARS-CoV-2 vaccine (red). The regulatory standards for standard and COVID-19 vaccine development are identical. The main differences include the compressed development time, the mobilization of several resources simultaneously, the expanded manufacturing capacity, allowing for the fast-tracking of COVID-19 vaccine development. The aim is to have the product available to use in a shorter period of time in comparison to the timeline of standard vaccine development and authorization.

IMMUNOTHERAPY

Cancer Therapies and ISRs

Immuno- and chemotherapeutics and oligonucleotide therapy against cancer are often administered in the form of injections. They undergo strict testing through clinical trials, which regulatory requirements include documentation and monitoring of potential as key components of the safety assessment procedure. Chemotherapeutics, in particular, are often classified as vesicants, which can cause severe reactions in the form of tissue necrosis or blister formation [11]. In various cases, immunotherapeutics can be associated with ISRs; oligonucleotides, for example, are always understood to be associated with ISRs [12].

Global Cancer Therapy Market

The worldwide burden of cancer is steadily increasing, and the disease is noted as the second leading cause of death. A 2021 American Cancer Society report states that in 2018, there were an estimated 17 million new cancer cases and 9.5 million deaths from cancer globally. By 2040, figures are expected to reach 27.5 million new cancer cases and 16.2 million cancer deaths due to the growth and aging world population [13]. Driven by a robust cancer therapeutics market estimated at over USD 160 billion globally, various drugs and treatments are developed to meet this demand [14].

Immunotherapies and chemotherapeutics hold a significant share of the global market. Cancer immunotherapy drugs account for nearly 50% of the overall oncology drugs market, generating approximately USD 75 billion in 2019 alone and forecast to surpass USD 143 billion by 2025 [15]. The global cancer immunotherapy market is spurred by the growing adoption of advanced cancer therapeutic options and the rising prevalence of cancer, leading to an estimated market value of USD 58.1 billion in 2018. The global cancer chemotherapy market is expected to grow at a CAGR of around 11.4% from 2020 to 2027 and reach a market value of more than USD 74.3 billion by 2027 [16].

At the same time, factors such as patient assistance programs, increasing government initiatives for cancer awareness, the rising prevalence of cancer worldwide, strong R&D initiatives, and demand for telemedicine are likely to support market growth [17].

Spotlight on Hybrid Clinical Trials

The growing prevalence of different types of cancer worldwide has led to increasing oncology medicine and research expenditure, driving the development of new products. The NCI's USD 120 million budget increase is exemplified for the fiscal year 2021 for Established and Early-Stage Investigators [18]. As the largest market, North America, particularly sees a rising increase in clinical trials to develop new drugs and treatments.

Worldwide, there are more than 1,000 ongoing clinical trials across different phases developing cancer treatment using immune-based therapies [19, 20]. Moreover, adverse effects associated with conventional chemotherapies are also driving the demand for standardized ISR tracking solutions. Several new immunotherapeutic options, including immunomodulators and CAR-T cell therapy, are currently being tested for their ability to provide improved cancer treatment [21], most notably for patients who are not responding to conventional chemotherapy.

Nevertheless, the current pandemic has harshly impacted cancer therapy development [22]. The latest Cancer Research Institute report states that as of April 1st, 2021, a total of 1130 trials listed on ClinicalTrials.gov were stopped due to COVID-19 -associated healthcare restrictions. Among them, upwards of 100 are listed as oncology trials [23]. Slow enrollment, enrollment suspension, and delayed initiation have been pertinent factors in clinical trial disruptions. At the pandemic's peak, 60% of institutions in the United States and 86% in Europe were enrolling new patients at a lower rate [24], and the majority of trials were listed as suspended rather than terminated.

Integrating novel digital health technologies as a solution for the steady revival and expansion into remote, home-based monitoring is currently driving the momentum for hybrid clinical trials. For more information on our telehealth solution [Telemedicine].

> "During Scarletred's participation in the EIT Health Gold Track Program, we supported their roll-out of a full-scope solution that addresses an unmet need in ISR monitoring a medical that allows the creation of an ISR database while providing the analytical tools necessary for an objective assessment of dermatological reactions."
>
> Christina Hertel, PhD
> Senior Program Manager
> Gold Track, EIT Health e.V.


DERMATOLOGY

DERMATOLOGY

Dermatology and ISR

The scope of injections in the dermatological field to treat diseases ranges from biologics over immunosuppressants to antibiotics. Common dermatological conditions where injectables are used for treatment and consequently ISRs become relevant include psoriasis, hidradenitis suppurativa (HS), and atopic dermatitis (AD), among others. Treatments of autoinflammatory diseases (e.g. psoriasis) include immunosuppressants where the parental administration route is favored over the oral one. The latter is associated with higher gastrointestinal symptoms in higher dosages and lack of compliance by patients [25]. Another class of injectable biologics, monoclonal antibodies, is administered to patients, for instance, suffering from very severe cases of AD [26]. Tracking of the injection site applies to substances administered intravenously and intramuscularly, subcutaneously, and intradermally.

Along with those treatments comes the possibility of developing adverse events from the injection itself and the substance being injected. The successful development of these injectables requires standardized ISR monitoring methods from the early pre-clinical development phases to human clinical trials and postmarketing studies since conventional assessment methods often lack objectivity, and documentation can be challenging [Table 1].

Global Injectables Market in Dermatology

The continuing expansion in the scope of research and applications and the increased demand for effective treatment methods and drugs contribute to the constantly growing global dermatology drugs market. In 2020, the global market size was at USD 37.57 billion and is forecast to grow at a compound annual growth rate (CAGR) of 12% to reach USD 62.83 billion in 2025, despite recovering from the reduced demand during the COVID-19 pandemic [27]. The leading regions in this market are Asia Pacific, with 36% of the market, followed by North America with 27%. The parenteral route of administration dominated the market in 2019 due to the approval of new biologics to treat various dermatological conditions, mainly psoriasis and AD. While effective surgical treatments are available for common conditions, drugs are preferred due to their easy availability [28].

The psoriasis market was valued at USD 13.4 million in 2020 and is expected to reach USD 23.6 million in 2026 with a CAGR of 9.89% [29]. The increasing disease burden, the demand for medicines to treat psoriasis in emerging economies, and the advancement in psoriasis research are the major factors driving the market's growth [29]. Psoriasis medication includes several different mechanisms of action and routes of administration, such as TNF-α inhibitors, PDE4 inhibitors, and biologicals targeting various interleukins (IL). The latter have shown particularly high safety and efficacy profiles and have seen rapid market growth.

In 2019, the global IL market size was at USD 18.22 billion and is expected to grow to USD 26.88 billion in 2023 at a CAGR of 14.44% after a 1.58% decline due to COVID-19 in 2020 [30]. Accordingly, since psoriasis represents the largest market share of IL inhibitors [31], antibodies targeting interleukins have been the most approved antibody drugs with a 46% growth in 2018 [29].

In hidradenitis suppurativa (HS), a chronic relapsing skin disorder, treatment includes immunosuppressants, antibiotics, and retinoids such as vitamin A derivatives [32, 33]. The HS market is expected to grow almost 50% from USD 898 million in 2018 to USD 1.81 billion in 2028 in the major markets, including the US, Germany, Italy, France, Japan, and the UK, at a CAGR of 7.2% [34].

The global market size of the chronic inflammatory skin condition, AD, was estimated at USD 11.7 billion in 2021 and is expected to reach USD 21.80 billion by 2026 with a CAGR of 13.13% [35, 36]. The growing incidences of skin allergies and chronic disorders contribute to the fast market growth rate. Furthermore, the increasing expenditure on healthcare and the growing popularity of treatments further accelerate the market growth [36].

Clinical trials of dermatological injections

Clinical trials are critical for advancement in medicine and can provide treatments to improve disease status and patients' quality of life. Biologics represent the future of therapeutics in dermatological conditions. These therapeutics have been most evaluated in psoriasis, and the first one to receive FDA approval for its treatment was in 2003 [37, 38]. The COVID-19 pandemic has significantly impacted clinical trials globally, resulting in the adoption of mobile digital skin imaging solutions such as Scarletred®Vision for use in virtual and hybrid trial models [39].

Currently, there are 84 active clinical trials, out of which 24 are recruiting, and 55 are in the final stages of testing globally for injectables to treat psoriasis [40]. The incidence of different ISRs can range from 16-75% for pain, 5-20% for erythema, and up to 13% for edema among 5 biologics used for moderate-to-severe plaque psoriasis [Figure 4] [41]. As mentioned above, IL inhibitors represent the fastest-growing group in the biologics market as psoriasis medication and are also gaining significance in treating HS. Injectable therapy for HS continues to be developed as the multifactorial pathogenesis of the condition is researched, and better understood [42]. In the last years, injected adalimumab has dominated the HS market; however, there are new injectable therapeutics on the way which can challenge its position [35]; there are 5 recruiting trials for HS worldwide, out of which 1 is in Phase III [41].

Regarding moderate to severe AD treatment, topical therapies are non-invasive but pose challenges in sufficiently controlling the condition. Thus, the development of targeted injectable biologics is essential [43]. In 2021, AD has only 1 biologic approved for patients, which can only be injected to be effective on the cellular level, making standardized monitoring crucial for safe testing [43]. However, there are currently 12 active clinical trials, out of which 6 are in Phase III, and 24 recruiting trials, out of which 8 are in Phase III for the development and testing of AD injectables [41].

Most drugs for these conditions are administered subcutaneously. Common side effects include typical ISRs (erythema, rash, edema, itching, or bruising), upper respiratory infections, headaches, and nausea, emphasizing precise monitoring during treatment and clinical testing [44].

According to clinical trial protocols, adverse events must be recorded regardless of severity and causality [45]. However, ISRs are often not actively tracked during trials of injectable drugs unless there are major red flags. These sometimes

only appear in larger cohorts and can cause ISRs of single individuals to go unnoticed. As adverse events differ individually and the dermatology market is continuously expanding, a standardized solution for monitoring ISRs is vital to ensure the patients' safety and well-being during treatment or clinical trials.

"The standardized monitoring of ISR is crucial for improving the quality of clinical trials using modern injectables in dermatology. Only unbiased data can inform physicians as well as patients and has the potential to further optimize care."

Christian Posch MD PhD
Board Certified Dermatologist

Figure 4. Proportion of ISR-related events in clinical trials regarding psoriasis. The incidence of ISRs can range from 16-75% for pain, 5-20% for erythema, and up to 13% for edema among five biologics used to treat moderate-to-severe plaque psoriasis [17]


COSMETICS

COSMETICS

Injectables and ISRs

ISR documentation and monitoring are necessary components of clinical trials for new injectable cosmetic products. Facial injectables are substances injected beneath the skin surface to reduce wrinkles, restore volume and fullness to the face, or improve the appearance of scarring. Some products are also used to treat various conditions such as neck spasms, excessive sweating, and eye-twitching [46]. Commonly used facial injectables include hyaluronic acid, botulinum toxin type A (Botox), and polymer fillers [47]. As patients turn to the cosmetic industry to improve their appearance, any local reaction is highly counterproductive. Nevertheless, it has been found that adverse reactions may become more common as new and more potent products, which include active ingredients, enter the market [48].

While the cosmetic industry typically faces fewer regulations than healthcare industries, this situation is shifting. Since May 2020, dermal fillers have been classed as medical devices under EU Medical Device Regulation 2017/745 [49]. Accordingly, safety assessment processes for cosmetic injectable products are currently evolving to meet these new standards.

Global Facial Injectables Market

The global facial injectable market size was valued at USD 13.4 billion in 2020 and is expected to increase significantly in the coming years [Figure 5]. Growing consciousness about physical appearance amongst populations and the increased availability of various products and procedures contribute to this market growth. Additionally, a shift in consumer preference toward minimally invasive procedures is boosting market growth due to their swift wound healing properties and visible treatment effects [50]. In 2019, Botox and soft tissue fillers were among the top 5 minimally invasive procedures carried out in the U.S. [51]. The combination of these factors reveals favorable prospects for the market. Higher demand for injectable treatments such as dermal fillers and Botox also increase the need for both on-site and remote ISR tracking methods.

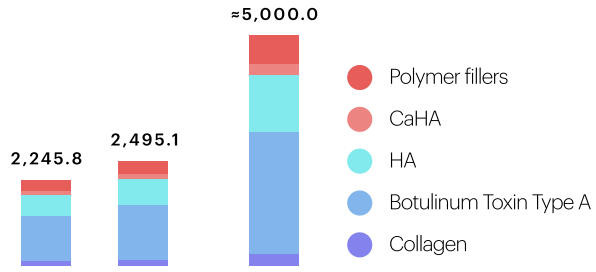


Figure 5: U.S. facial injectable market size, by product, 2016 - 2027 in USD Billion - Grandview Research

Experts estimate that the cosmetic market is about ten times bigger than the vaccine market due to its capacity to produce more products in a shorter time frame. As cosmetic products typically require less time for development and are subject to fewer regulations, cosmetic companies can produce approximately 10-20 products a year compared to the single vaccine that a biopharmaceutical company might develop in the same time period.

One of the main challenges of this market is that a considerable number of formulas must undergo testing for each product resulting in a sizable volume of trials that need to be carried out before a new product can be released. Moreover,

new regulations such as the EU Medical Device Regulation 2017/745, demand increased accuracy and effectiveness during trials. This frequency of testing combined with market projections emphasizes the need to streamline processes and reduce professionals' workloads by employing standardized tools to support them through the sheer volume of trials.

As cosmetic procedures are becoming more popular and accessible, there is a clear economic interest in the cosmetic injectables industry. Companies are expected to deliver failure-proof products which meet customer expectations. Improved management of the side-effects of new products proves to be a critical opportunity for companies' further growth. One way of dealing with this is by monitoring ISRs as closely as possible, is to document and identify their intensity and duration, both during the testing and post-marketing phases.

	SITE EFFECTS	SIDE EFFECTS	PROBABILITY
Botox	Swelling - Bruising - Itching - Skin Thightness - Skin Rash	Dizzines - Wheezing - Death of Skin Cells - Embolism	1% - 5%
HA HYALURONIC ACID	Redness - Itching - Swelling - Bruising	Pain - Blindness	Not Found
CaHA CALCIUM HYDROXYAPATITE	Swelling - Bruising - Bleeding - Lumps and Bumps - Redness - Scarring	Vascular Occlusion - Blindness	Not Found

Table 3. Overview of commonly used beauty injections, their side effects, site effects and probability of occurrence.

Rates of ISRs can be relatively high in the cosmetic injectables industry since local sites must be injected multiple times throughout treatment. Botox injections, in particular, are a popular cosmetic procedure nationwide in the United States. In 2019, over 7.5 million people underwent Botox treatments [Table 3] [52]. For effective results, Botox treatments must be carried out regularly every 3 - 12 months. Some practitioners report injecting an average of 10 to 30 units into the forehead per session. Botox manufacturer, Allergan, recommends a dosage of four units, each in five sites on the forehead, totaling 20 units per session. Glabellar lines administration has five approved facial injection sites, whereas lateral canthal lines administration is authorized for three sites [53]. Limited authorized injection sites and the repeated placement of a needle into these areas can easily result in strong local ISRs.

Thus, mitigating these reactions by efficient documentation and monitoring methods is of utmost importance and can boost competitive advantage and increase customer satisfaction. Moreover, during post-injection recovery, individuals, as well as doctors, greatly benefit from having a scalable and user-friendly digital tool that allows daily tracking of injection sites by patients from their homes, saving time and costs and increasing positive treatment outcomes. For more information on our telemedicine solution: [Telemedicine].

Diversity in the Cosmetic Industry

The cosmetic industry is constantly developing new products for different skin tones and is challenged in monitoring their effects, which, depending on the skin tone, have different appearances. For example, in 2017, Fenty Beauty debuted with cosmetic foundations for 40 skin tones and later increased this number to 50 shades, employing this product diversity as its unique selling point. The company was reported to have garnered 100 million USD in its first 40 days, sharply accelerating a growing trend towards inclusivity with several brands following suit to capture the market [54]. Moreover, L'Oréal has long been involved in expanding its range of products to people of different ethnicities. The company reports investing 3.5% of its revenue in R&D, backing dedicated multicultural beauty

facilities, and seeing considerable success [55]. As the market expands to create products for clients of various ethnicities across the pigmentation spectrum, a need to enhance clinical trial processes has become apparent. Skin reactions caused by products designed for an increased range of skin types must be tracked carefully as erythema, and ISRs, in general, appear differently on varying skin tones. Professionals continuously report the challenge of comparing reactions on differing pigmentation levels. So far, a lack of tools that allow for objective comparison potentially leads to skin reactions on certain skin types being overlooked during testing. It is evident that the cosmetic field would highly benefit from improved product quality by tackling this issue. For a company to substantially include diversity in its product portfolio and thus, successfully capture this growing market, digital tools that allow for standardization, analysis, and comparison between different ethnicities are proving to be essential. In this context, in addition to erythema quantification, SCARLETRED has integrated the measurement of the individual typology angle (ITA°) to its toolkit to produce high-quality images along with the quantification of skin pigmentation alterations [Figure 6].

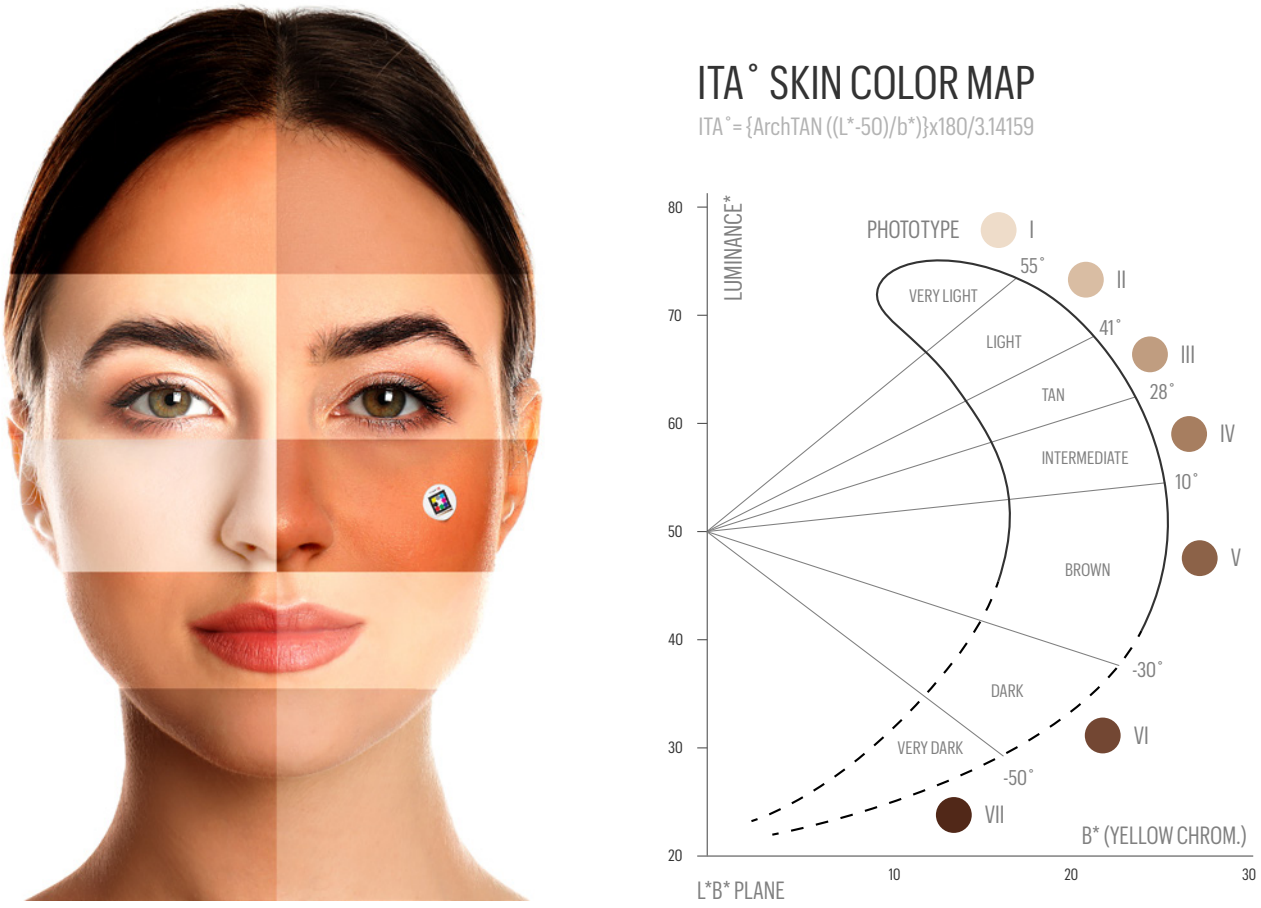


Figure 6. Individual Typology Angle (ITA°) skin color map.


TELEMEDICINE

TELEMEDICINE

The ongoing pandemic has led to a disruption of several clinical trials, revealing the need for remote means of investigation. One of the reasons behind clinical trials coming to a halt is the shutdown of hospitals to non-staff and non-emergency patients, including patients participating in clinical trials.

Patients with movement hindrances or higher susceptibility to infections are even more affected as physical interaction is highly discouraged. Therefore, the solution is to implement a scalable digital telemedical solution that both doctors and patients can use, in-clinic and at-home, which houses a real-time high-quality documentation platform and provides remote consultation services.

Reports of delayed ISRs of up to or exceeding eight days following vaccination administration suggest a need for continued monitoring to characterize them properly [56]. This claim is supported by professionals in the pharmaceutical industry, who have predicted that remote patient monitoring will be the growing trend with the most impact in 2021 [57].

ISR Tracking through Remote Home-Based Monitoring

As a type of telehealth, remote patient monitoring enables healthcare professionals to receive patient-specific information remotely in real-time and on a secure platform, eliminating the need for patients to travel to the clinic. Social distancing requirements during the pandemic have led to a more recent push for digital, remote solutions, which was preceded by the efforts of various stakeholders to improve care for vulnerable patients and those with limited movement abilities. Out of necessity during the COVID-19 crisis, healthcare processes and clinical trials have seen a sharp uptick in the use of remote telemonitoring solutions along with other digital health technologies [Figure 7] [58]. According to GlobalData, the remote patient monitoring market is expected to benefit substantially from this shift and is predicted to surpass USD 645 million by 2025 [59]. This growth is also supported by an increase in the chronic disease population and the aging population as these solutions significantly aid them.

The demand for home-based monitoring devices is evident. Telehealth usage was estimated to have increased 300-fold during the pandemic [60], and across all age groups, a high adoption rate revealed the simplicity of operating many home-based devices. Furthermore, a study of U.S. based staff at 25 pharmaceutical or biotechnology organizations of varying sizes

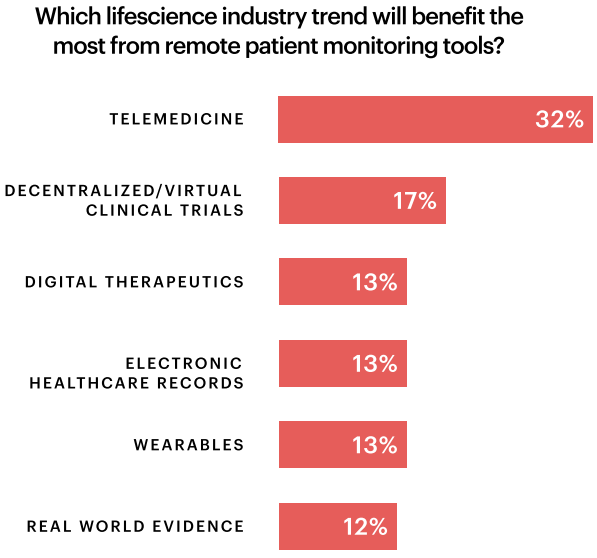


Figure 7: A 2021 poll from Verdict assessing which of the life sciences industry trends will benefit the most from remote patient monitoring tools. - Pharmaceutical Technology

found that telemedicine was among the most frequently adopted technologies by companies running clinical trials during the pandemic [61]. The majority of the organizations have adopted telehealth, primarily for routine follow-ups in Phase I studies to identify adverse events.

Telemonitoring was also used to assess factors such as the size of lesions in dermatology trials [62]. Another poll conducted by Verdict revealed that 64% of respondents who were clinical research professionals are planning to amend their future trial protocols to include remote monitoring [63]. 88% of healthcare providers were shown to have invested in or already consider adopting remote patient monitoring devices in another survey [64]. As patients and pharmaceutical industries have suffered from treatment disruptions and clinical trial delays, the adoption of telehealth and other supportive technology is a key driver in the industry's recovery. The COVID-19 crisis has necessitated the use of remote monitoring tools to continue clinical trials without risking public health and thus resulted in their extensive implementation [65]. Current challenges shed light on the benefits of adequately incorporating such tools and technologies.

The Golden Age for Decentralized Trials

The evident benefits of remote, home-based monitoring tools could make a case for a higher prevalence of decentralized clinical trials. As COVID-19 vaccine research continues, cohort-specific considerations must be made as older populations are understood to be at higher risk, and pediatric vaccination research entails new challenges [66,67]. Clinical trial adjustments that provide higher accessibility for members of these groups may prove to be highly beneficial. Moreover, recent reports suggest that clinicians may not be prepared to address delayed local reactions from the mRNA-1273 vaccine [68]. This presents a problem for the characterization and classification of ISR developments amongst other delayed reactions. The implementation of more efficient technology will be required as continued safety monitoring of vaccines is undertaken, particularly in post-approval phases [69].

Additionally, as the current situation still entails limited contact, there is a need for off-site trial components (hybridization of trials) or completely decentralized trials. These can be leveraged to ensure consistent monitoring of participants even when in-person care is not possible. Still, it has been reported that certain technical requirements for running decentralized trials can make them infeasible for specific therapies or diseases with the most commonly known technologies.

As fully decentralized and hybrid trials become more common, they may also address several challenges that traditional clinical trials have historically faced. Decentralized trials could help increase trial access and participant diversity as the traditional lack of geographically diverse sites excludes important demographics [70, 71]. Furthermore, a 2009 study from the National Academy of Sciences found that 75% of drug research costs are sunk in products that fail to move out of the clinical trial phase [72].

Decentralized trials offer lower costs and the opportunity to mitigate loss, and are becoming essential for industries to recover from the current setbacks. For these trials to be effective and viable, efficient remote monitoring tools must be implemented. Therefore, there is a clear need for industries to adopt already available innovative digital tools which are efficient, effective, scalable, and user-friendly.

OUR SOLUTION

OUR SOLUTION FOR ISR MONITORING

The main difficulty in tracking ISRs lies on the one hand in the practicality, rentability, and scalability of the methods used and, on the other hand, on the timing. After the injection, patients may spend a short amount of time in the clinic to ensure that they do not have any immediate strong physiological reactions to the injected substance. The study staff or doctor himself can visually monitor the injection site during this time. Nevertheless, ISRs tend to evolve hours, days, and even weeks after the injection has taken place, entailing that medical professionals and industries rely solely on the patient to monitor and report potential reactions around the injection site (of which they often do not have a clear view) on a specific platform, rendering ISR tracking very difficult to carry out. The Scarletred®Vision technology simplifies this process and empowers doctors and patients alike to create a high-quality real-time database that is crucial to the development of safe injectables.

WHAT IS SCARLETRED®VISION?

Scarletred®Vision is SCARLETRED's state-of-the-art CE-certified medical device, enabling high-quality standardized imaging, centralized data management, and objective analysis of dermatological conditions. The technology allows for professionals to document, assess, and quantify skin alterations resulting from a disease, allergic reactions, drug reactions, trauma, and last but not least, injections. Scarletred®Vision is a CE-certified Class I Medical Device and is ICH- GCP, GDPR, and HIPAA compliant. The proprietary technology is developed and supplied in accordance with ISO-13485 Quality Management System.

Scarletred®Vision is implemented in various settings, including drug development in clinical trials (preclinical to phase IV), routine clinical work, hospital care, and remote home-based patient monitoring. The integrated analytical and AI-powered tools are configured according to the goals of the individual study, and features can be optimized for the specific use case or according to the clinician's requirements. Patient-specific data that could lead to their identification is neither entered into nor stored on Scarletred®Vision, ensuring patient privacy and anonymity.

Scarletred®Vision enhances current practices by removing the administrative tasks and inconveniences involved in traditional methods of ISR monitoring, owing to the following advantages:

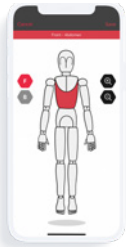
- Generation, documentation, & management of standardized and calibrated dermatological images
- Real-time and delayed scoring
- Quantitative analysis of erythema and surface area
- Research Tools: customizable AI-powered tissue classification and Machine Learning
- The facilitation of subject eligibility evaluation
- The sharing of images among professionals without having to send images and data
- The establishment of independent and anonymous comparative scoring of
- a patient's skin condition by different professionals
- Implemented in preclinical to phase IV clinical trials

HOW IS SCARLETRED®VISION APPLIED IN ISRs?

The Scarletred®Vision Medical Device consists of 4 components:

Scarletred® QR Codes

Used to create patient dossiers and take patient images; each patient is assigned a unique QR. Ensures patient data privacy and blinding: patients remain anonymous, and information that could be used to identify patients is not stored on Scarletred®Vision. Only the treating doctor holds the de-anonymization key. Data can be unblinded in a controlled procedure.

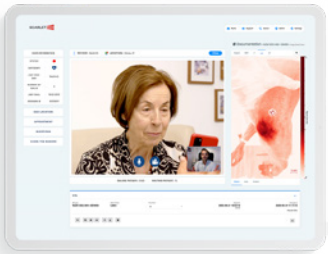


Scarletred® Mobile App

The app is developed and tested in clinical trials with medical experts and allows to convert a GCP compliant process in your clinical trial and medical routine applications. Upon request, we offer a 100% controlled remote service in which we supply the latest iPhone models with the Scarletred®Vision App pre-installed to the client directly. This includes a remote managed service.

Scarletred® Skinpatch

Our patented Scarletred®Vision Skin Patch is automatically detected by the Scarletred®Vision App and allows normalizing taken skin images by color and size in a GCP-compliant process. The biocompatible adhesive film allows mounting of the patch even on very sensitive skin.



Scarletred® Online Platform

It is an online dermatological imaging platform for image data management and analysis and the main component of the medical device. Previously generated dermatological images can be transferred to the Scarletred®Online platform remotely from the Scarletred®Mobile app.

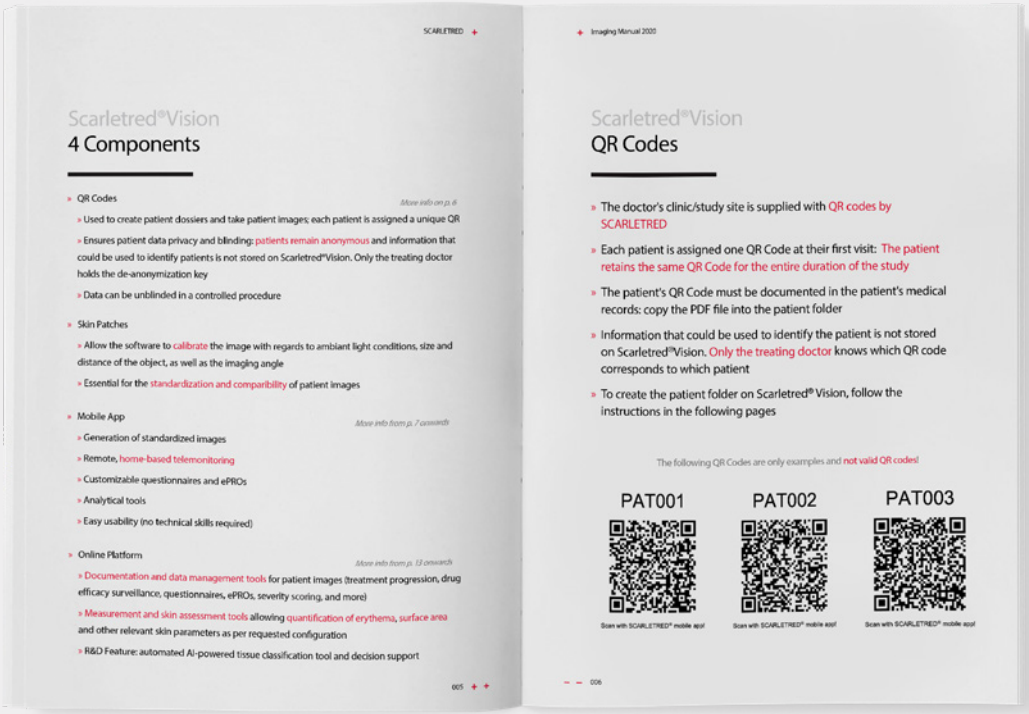
Overview
Objective Digital Dermatology

Our CE-certified Class I medical device product Scarletred®Vision is ICH-GCP- and GDPR-compliant and solves the problem of lacking standardization and objectivity in Teledermatology

- Generation, documentation, & management of standardized and calibrated dermatological images
- Real-time and delayed scoring
- Quantitative analysis of erythema and surface area
- Research Tools: customizable AI-powered tissue classification and Machine Learning
- The facilitation of subject eligibility evaluation
- The sharing of images among professionals without having to send images and data
- The establishment of independent and anonymous comparative scoring of a patient's skin condition by different professionals
- Implemented in pre-clinical to phase IV clinical trials

IMAGING MANUAL AND IMPLEMENTATION GUIDE

For Biopharma, Cosmetics, and Telemedicine



SCARLETRED

Scarletred®Vision
4 Components

- QR Codes *More info on p. 6*
  - Used to create patient dossiers and take patient images; each patient is assigned a unique QR
  - Ensures patient data privacy and blinding: patients remain anonymous and information that could be used to identify patients is not stored on Scarletred®Vision. Only the treating doctor holds the de-anonymization key
  - Data can be unblinded in a controlled procedure
- Skin Patches
  - Allow the software to calibrate the image with regards to ambiant light conditions, size and distance of the object, as well as the imaging angle
  - Essential for the standardization and comparibility of patient images
- Mobile App *More info from p. 7 onwards*
  - Generation of standardized images
  - Remote, home-based telemonitoring
  - Customizable questionnaires and ePROs
  - Analytical tools
  - Easy usability (no technical skills required)
- Online Platform *More info from p. 13 onwards*
  - Documentation and data management tools for patient images (treatment progression, drug efficacy surveillance, questionnaires, ePROs, severity scoring, and more)
  - Measurement and skin assessment tools allowing quantification of erythema, surface area and other relevant skin parameters as per requested configuration
  - R&D Feature: automated AI-powered tissue classification tool and decision support

005

Imaging Manual 2020

Scarletred®Vision
QR Codes

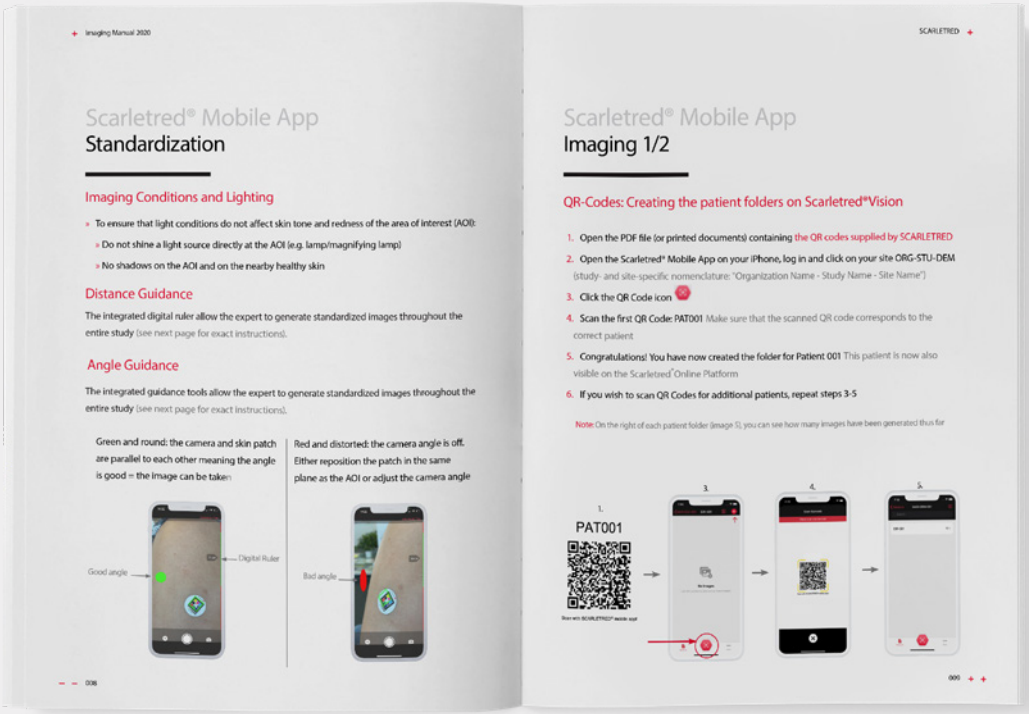
- The doctor's clinic/study site is supplied with QR codes by SCARLETRED
- Each patient is assigned one QR Code at their first visit: The patient retains the same QR Code for the entire duration of the study
- The patient's QR Code must be documented in the patient's medical records: copy the PDF file into the patient folder
- Information that could be used to identify the patient is not stored on Scarletred®Vision. Only the treating doctor knows which QR code corresponds to which patient
- To create the patient folder on Scarletred® Vision, follow the instructions in the following pages

The following QR Codes are only examples and not valid QR codes!

PAT001 PAT002 PAT003

Scan with SCARLETRED® mobile app! Scan with SCARLETRED® mobile app! Scan with SCARLETRED® mobile app!

006



Imaging Manual 2020

Scarletred® Mobile App
Standardization

Imaging Conditions and Lighting

- To ensure that light conditions do not affect skin tone and redness of the area of interest (AOI):
  - Do not shine a light source directly at the AOI (e.g. lamp/magnifying lamp)
  - No shadows on the AOI and on the nearby healthy skin

Distance Guidance

The integrated digital ruler allow the expert to generate standardized images throughout the entire study (see next page for exact instructions).

Angle Guidance

The integrated guidance tools allow the expert to generate standardized images throughout the entire study (see next page for exact instructions).

Green and round: the camera and skin patch are parallel to each other meaning the angle is good = the image can be taken

Red and distorted: the camera angle is off. Either reposition the patch in the same plane as the AOI or adjust the camera angle

Good angle Digital Ruler Bad angle

008

SCARLETRED

Scarletred® Mobile App
Imaging 1/2

QR-Codes: Creating the patient folders on Scarletred®Vision

1. Open the PDF file (or printed documents) containing the QR codes supplied by SCARLETRED
2. Open the Scarletred® Mobile App on your iPhone, log in and click on your site ORG-STU-DEM (study- and site-specific nomenclature: "Organization Name - Study Name - Site Name")
3. Click the QR Code icon
4. Scan the first QR Code: PAT001 Make sure that the scanned QR code corresponds to the correct patient
5. Congratulations! You have now created the folder for Patient 001 This patient is now also visible on the Scarletred Online Platform
6. If you wish to scan QR Codes for additional patients, repeat steps 3-5

Note: On the right of each patient folder (image 5), you can see how many images have been generated thus far

1. PAT001 3. 4. 5.

009

Scarletred® Mobile App
Imaging 2/2

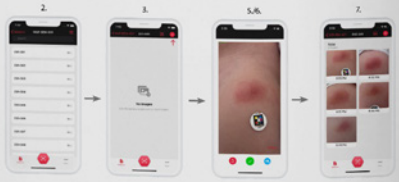
Taking the Images

1. Place the Scarletred® Skin Patch on the healthy skin, next to the area of interest
2. Select and open the patient's folder
3. Click on the plus sign to open the camera
4. Click on the capture image icon to take a picture*
5. Review and ensure that the image is suitable for assessment (according to your requirements).
6. Click the green icon to save the image OR the undo icon to re-take the image . To take another image of the same patient, click on the icon.

Once the image has been saved, it cannot be deleted from the Scarletred® Online Platform and the Mobile App

7. After saving the image(s), an overview of all images for this patient will be displayed (incl. time and date)

Note: If the capture image button is not clickable (greyed-out), it means that the Scarletred® Skin Patch has not been detected -> adjust the framing



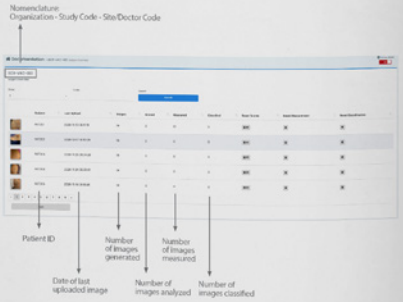
Scarletred® Mobile App
Questionnaires and ePROs

Study-Specific Configurable

- Questionnaires and ePROs can be configured to appear at specific frequencies: e.g. after an image has been generated, on a daily, weekly, or monthly basis. Multiple questionnaires can also be configured.
  - Examples: DLQI, QoL, Insomnia Score, Itch Score, eVIP (Vaccination Injection Perception), and more.
- They can be configured according to the physician's/study requirements and can be used for:
  - In-clinic assessments
  - At home remote monitoring: depending on the study design, patients can take daily images of selected lesions from their home and automatically have a questionnaire pop-up. The doctor can consequently monitor the success of the treatment plan much more closely without needing the patient to come in to the clinic every day
- Results and answers can be visualized on the online platform (refer to p.16 for more details)
- Example of an in-app patient ePRO following the injection in a vaccine clinical trials:

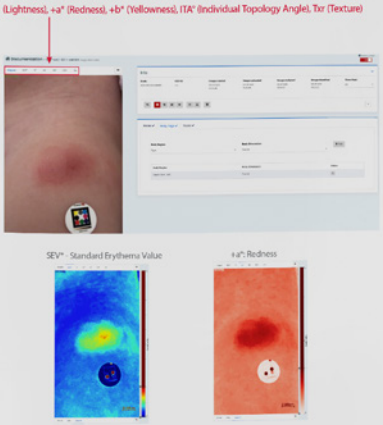
Scarletred® Online Platform
Documentation 1/2

- Once signed in, you will have access to your assigned sites and all therewith related data
- Click on the site of interest to see the list of all photographed patients from this site. For each patient, information about the number of images generated, the number of images analyzed, and the date of last uploaded image are displayed



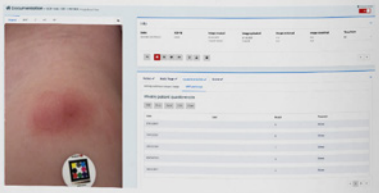
Scarletred® Online Platform
Augmented Visualization

- Signal Map: The patient's images can be displayed in 6 different map signals, each useful to augment the visualization of different skin parameters : SEV* (standard erythema value), L* (Lightness), +a* (Redness), +b* (Yellowness), ITA° (Individual Topology Angle), Txr (Texture)



Scarletred® Online Platform
Questionnaire & ePRO Results

- Results from the in-app questionnaire can be visualized by the treating physician on the online platform:
  - In the vaccination study below, 2 ePROs were configured: an Itch and Insomnia patient self-reported outcome questionnaire and the eVIP, which appear after an image has been generated. Alternatively questionnaires can also be configured to appear on a daily, weekly, or monhtly basis
  - The automatically calculated resulting index is displayed for each time point
  - To see answers to specific questions, the dermatologist can simply click on "Show" and the patient's answers to all questions drop-down



Scarletred® Online Platform
Erythema Quantification: Drawing the AOIs

- 1) Click on the the measurement icon (1)
- 2) To draw and select the treated areas on the image:
  - a) Click on the draw icon (2) next to the corresponding treatment area
  - b) Select the drawing shape: square, circle, or polygone (3)
  - c) Draw around the injection site on the image
- Repeat Step 2) in case of multiple injection areas and click on the checkmark icon (4) to conclude the measurement and see the results

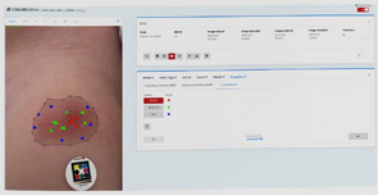
Scarletred® Online Platform
Erythema Quantification : Results

- For each selected treatment area, the following parameters are listed in the results table:
  - 1- Surface area; 2- SEV= Standard Erythema Value; 3- Lightness; +a*: Redness; +b*: Yellowness; 4- Delta E; 5- Individual Topology Angle ITA°; 6- Texture Txr

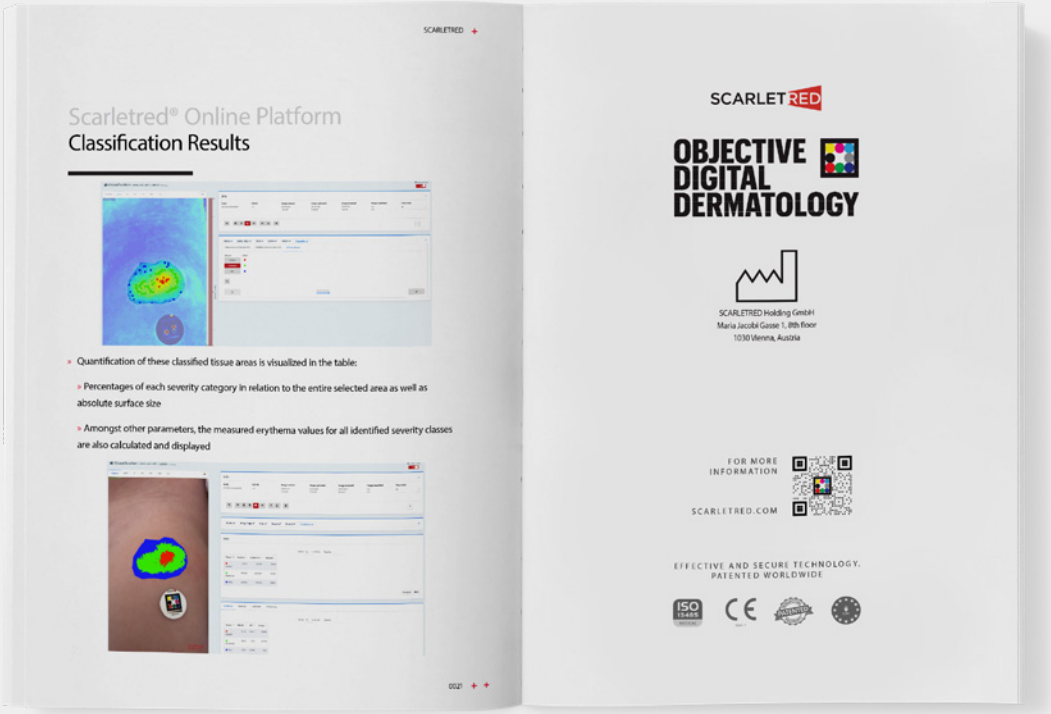
- It is recommended to quantify erythema using the values of the SEV* fold increase with reference to the local reference value (area-specific doted circle), which itself corresponds to the healthy, untreated skin
- Data visualization: the "Plot" tab presents the progression of a specific paramater (e.g. surface area, erythema) over flagged or all timepoints:

Scarletred® Online Platform
AI-Powered Classification

- Scarletred®Vision offers an A.I.-powered classification intended to automatically classify and quantify skin areas with different colors and/or textures with minimal input by the expert, resulting in a highly effective, efficient, and precise data analysis
- The goal is to teach the software to recognize specific types of tissues with minimal input by the expert
- The expert can conduct the analysis either using the original image (screenshot below) or the image in the augmented SEV visualization map (screenshot next page). The advantage of assessing ISRs in the SEV map is that the erythema severity degrees can be much more easily identified.



- First, the ISR area is selected and a few representative areas of the pre-defined different severity degrees (mild, moderate, severe) are selected by the expert: this input is then used by the AI to learn to recognize the other areas in this image that have the same color and texture. Consequently, the technology is then able to find and classify the rest of the image according to the initial input given by the user.



Let's work together

SCARLETRED is committed to collaborating and engaging with the professional community across all industries on a global level: biopharma & cosmetic industries, hospitals, CROs, clinics, and more. Its modular architecture and scalability render it the perfect fit for both small companies and established multinationals.

Austrian companies leading in the life sciences currently have several promising drugs and vaccines in the pipeline. These include Apeiron, Apeptico, Cebina, Cyprumed, F4 Pharma, G.ST Antivirals, Innophore, Marinomed, Panoptes, Polymun, Takeda, Valneva, and Viravaxx [72].

Request ISR SaaS package

We would like to hereby encourage collaboration by offering the Scarletred®Vision SaaS technology at a special rate for ISR applications. Whether you are a newcomer or an established large corporation, get in touch with us so we can find the best suitable solution to fit your requirements.

For business inquries
office@scarletred.com

For marketing inquries
marketing@scarletred.com

WHO WE ARE

WHO WE ARE

SCARLETRED was founded in Austria in 2014 by Dr. Harald Schnidar, MBA, with the aim of introducing standardization in the process of medical data generation, objectify disease & treatment assessment and accelerate data analysis in clinical trials & routine.

SCARLETRED Holding GMBH

The scale-up's headquarters is located in Vienna's Biocenter, a cluster for life sciences where renowned academic research institutes and young and established pharmaceutical and biotechnology companies all have their offices close quarters to promote the exchange of ideas and collaborations. SCARLETRED also has offices in Cambridge, Massachusetts, USA, to facilitate and promote US-based projects.

SCARLETRED strives to solve some of the main challenges in dermatology, namely providing doctors and experts with convenient, easy-to-use, and scalable digital health tools that enable them to generate standardized documentation and objective quantitative diagnosis processes.

To ensure compliance across the board, Scarletred®Vision maintains industry standards: it is a CE-certified Class I Medical Device, ICH-GCP, GDPR, and HIPAA compliant, and holds ISO 13485 Quality Management System certification, making it fully equipped to provide the technology for the development of healthcare and skincare products at a faster rate while significantly saving costs, from the pre-clinical phases to the post-marketing surveillance studies and routine clinical work. The scalable solution is offered in a fair and affordable SaaS package tailored to the client's needs, thereby making it adequate for both young start-ups and established multinational companies.

In March 2020, SCARLETRED swiftly developed the certified telemedicine app and web-based platform, eCOVID19, to help manage the onset of the SARS-CoV-2 crisis, introducing the software as a decision support solution solution and symptom self-assessment verifier to support the national pandemic hotline and provide a communication platform via secure video call, opening the door for Telehealth and remote, home-based consultations.

SCARLETRED

GDPR

MEDICAL DEVICE ISO 13485

CE Class I

HIPAA COMPLIANT

ICH GCP 100% COMPLIANT

INTELLECTUAL PATENTED PROPERTY

OUTLOOK

The overviews presented highlight the mounting challenges faced by the pharmaceutical and cosmetic industries regarding ISR monitoring, covering a broad spectrum of treatments and therapeutics that are in dire need of innovative and scalable digital tools that combine in-clinic requirements while at the same time facilitating easy patient telemonitoring. The SARS-CoV-2 pandemic has emphasized the importance of remote, home-based monitoring capacity required not only for clinical trials, but also for routine medical check-ups: for the more vulnerable population, this symbolizes a relief for a long-awaited and unmet need; from the medical professionals' perspective, Scarletred®Vision materializes the opportunity to increase the accuracy of treatment and close tracking of disease progression by enabling remote monitoring; as for pharmacies, telehealth services enable their clients and customers to reach them from the comfort of their home. Streamlining product development with reliable and scalable innovative tools is of the utmost importance to applicable industries as they take on growing market opportunities in addition to meeting changing global standards, which have been accelerated by, amongst other reasons, the impact of the SARS-CoV-2 pandemic. Constructive steps forward will entail crucial improvements of the clinical trial processes by acknowledging the challenges that professionals in the affected industries have voiced. Enhancing ISR monitoring and assessment methods in clinical trials and various other settings is possible by implementing innovative state-of-the-art technology offered by Scarletred®Vision.

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GREEN ROCKET

Funded by the European Union

REFERENCES

1. Injection Site Reactions and How to Manage Them. Pharmacy Times: Immunization Guide for Pharmacists. November 2019, 1 (5). Retrieved April 20 2021 from: https://www.pharmacytimes.com/view/injection-site-reactions-and-how-to-manage-them.

2. Gault, D. Extravasation Injuries. British Journal of Plastic Surgery. 1993. 46: 91-96

3. Injection Site Reactions. Oncolink. July 22 2020. Retrieved April 20 2021: https://www.oncolink.org/cancer-treatment/cancer-medications/cancer-medication-safety/injection-site-reactions

4. Shimabukuro, Tom. COVID-19 Vaccine Safety Update. National Center for Immunization & Respiratory Diseases. January 27 2021.

5. Vaccines Market Size, Share & COVID-19 Impact Analysis. Fortune Business Insights. Retrieved April 20 2021 from: https://www.fortunebusinessinsights.com/industry-reports/vaccines- mar ket-101769

6. Wang, Hong-Peng et al. Current Status and Future Trends of Vaccine Development Against Viral Infection and Disease. New Journal of Chemistry. Mar 30 2021. https://doi.org/10.1039/ D1NJ00996F

7. Global COVID-19 Vaccine Market Outlook and Forecast 2021-2024: Emergence of Next-Generation Vaccine Platforms & Contract Manufacturers Accelerating COVID-19 Vaccine Production. Retrieved April 20 2021 from: https://www.prnewswire.com/news-releases/global-covid-19-vaccine-market- out look-and-forecast-2021-2024-emergence-of-next-generation-vaccine-platforms--contract-manufactur ers-accelerating-covid-19-vaccine-production-301256722.html

8. The European Medicines Agency (EMA). Retrieved April 20 2021 from https://www.ema.europa.eu

9. Zimmer et. al. Coronavirus Vaccine Tracker. The New York Times. Retrieved April 20 2021 from: https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

10. D'souza et al. What is Herd Immunity and How Can We Achieve It With COVID-19?. John Hopkins University Bloomberg School of Public Health. April 6 2021. Retrieved April 20 2021 from: https://www.jhsph.edu/covid-19/articles/achieving-herd-immunity-with-covid19.html

11. Kreidieh et al. Overview, Prevention and Management of Chemotherapy Extravasation. World Journal of Clinical Oncology. February 10 2016; 7(1): 87–97

12. 12. Van Meer et al. Injection Site Reactions after Subcutaneous Oligonucleotide Therapy. 2016 Aug; 82(2):340-51. https://doi.org/10.1111/bcp.12961

13. Cancer Facts and Figures 2021. American Cancer Society. 2021. p52. Retrieved April 20 2021 from:https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf

14. 2020 Global Cancer Immunotherapy Market Analysis & Forecasts. Businesswire. November 12 2020. Retrieved April 20 2021 from: https://www.businesswire.com/news/home/20201112005587/en/2020-Global-Cancer-Immunotherapy-Market-Analysis-Forecasts-A-143-Billion-Market-by-2025--- Re searchAndMarkets.com

15. 2020 Global Cancer Immunotherapy Market Analysis & Forecasts. Businesswire. November 12

2020. Retrieved April 20 2021 from: https://www.businesswire.com/news/home/20201112005587/en/2020-Global-Cancer-Immunotherapy-Market-Analysis-Forecasts-A-143-Billion-Market-by-2025--- ResearchAndMarkets.com

16. Cancer Chemotherapy Market Value Anticipated To Reach US$ 74.3 Billion By 2027. Acumen

17. Research and Consulting. February 8 2021. Retrieved April 20 2021 from: https:// www.globenewswire. com/news-release/2021/02/08/2171622/0/en/Cancer-Chemotherapy-Market- Value-Anticipated-To Reach-US-74-3-Billion-By-2027-Acumen-Research-and-Consulting.html

18. Cancer Therapy Market - Growth, Trends, COVID-19 Impact, and Forecasts (2021 - 2026). Mordor Intelligence. Retrieved April 20 2021 from:https://www.mordorintelligence.com/industry-reports/cancer-therapy-market

19. NIH and NCI Funding Increased in FY 2021 Budget Deal. American Cancer Society Cancer Action Network. December 21 2020. Retrieved April 20 2021 from: https://www.fightcancer.org/releases/nih- and-nci-funding-increased-fy-2021-budget-deal-access-care-prioritized

20. Cancer Immunotherapy Market - Growth, Trends, COVID-19 Impact, and Forecasts (2021-2026). Mordor Intelligence. Retrieved April 20 2021 from: https://www.mordorintelligence.com/industry- reports/cancer-immunotherapy-market

21. COVID Research Updates: Older People are at Higher Risk of Getting COVID Twice. Nature. March 19 2021. Retrieved April 20 2021 from: https://www.nature.com/articles/d41586-020-00502-w

22. Cancer Immunotherapy Market - Growth, Trends, COVID-19 Impact, and Forecasts (2021-2026). Mordor Intelligence. Retrieved April 20 2021 from: https://www.mordorintelligence.com/industry- reports/cancer-immunotherapy-market

23. Buckley-Mellor, Oliver. What's Happened to Cancer Clinical Trials During the COVID-19 Pandemic?. Cancer Research UK. November 4 2020. Retrieved April 28 2021 from: https:// scienceblog.cancerresearchuk.org/2020/11/04/whats-happened-to-cancer-clinical-trials-during-the- covid-19-pandemic/

24. CRI Anna-Maria Kellen Clinical Accelerator: COVID-19 and Clinical Trials. Cancer Research Institute. April 1 2021. Retrieved April 20 2021 from: https://www.cancerresearch.org/scientists/ immuno-oncology-landscape/covid-19-oncology-clinical-trials

25. Balfour, Hannah. COVID's Impact on Cancer Therapeutics: Clinical Trial and Treatment Disruptions. European Pharmaceutical Review. February 19 2021. Retrieved April 20 2021 from: https://www.europeanpharmaceuticalreview.com/article/143162/covids-impact-on-cancer- therapeutics-clinical-trial-and-treatment-disruptions/

26. Leis-Dosil, V. M., & Prats-Caelles, I. Practical management of immunosuppressants in dermatology. Actas Dermo-Sifiliográficas (English Edition), 2018 Jan-Feb; 109(1): 24-34. https://doi.org/10.1016/j.adengl.2017.11.004

27. Din, Ahsan Tameez Ud et al. Dupilumab for Atopic Dermatitis: The Silver Bullet We Have Been Searching for? Cureus. 2020 Apr 6. https://doi.org/10.7759/cureus.7565

28. Dermatology Drugs Global Market Report 2021 - By Type (Acne, Dermatitis, Psoriasis, Other

Drugs For Dermatology Diseases), By Distribution Channel (Hospital Pharmacies, Retail Pharmacies/ Drug Stores, Others), By Route Of Administration (Oral, Parenteral, Others), By Drug Classification (Branded Drugs, Generic Drugs), By Mode Of Purchase (Prescription-Based Drugs, Over-The-Counter Drugs), COVID-19 Impact And Recovery. The Business Research Company. Retrieved August 24 2021 from: https://www.thebusinessresearchcompany.com/report-preview1.aspx?Rid=dermatology%20drugs%20global%20market%20report%202020%2030%20covid%2019%20impact%20and%20recovery

29. Dermatology Drug Market- Global Industry Analysis, Size, Share, Growth, Trends and Forecast 2016-2024. Retrieved August 26 2021 from: https://www.transparencymarketresearch.com/dermatology-drug-market.html

30. Psoriasis Drugs Market - Growth, Trends, COVID-19 Impact, and Forecasts (2021-2026) Mordor Intelligence. Retrieved August 24 2021 from: https://www.mordorintelligence.com/industry-reports/psoriasis-drugs-market

31. Interleukin Inhibitors Global Market Report 2020-30: COVID-19 Growth and Change. The Business Research Company. December 2020. Retrieved August 26 2021 from: https://www.researchandmarkets.com/reports/5228419/interleukin-inhibitors-global-market-report-2020?utm_source=BW&utm_medium=PressRelease&utm_code=qzbn7x&utm_campaign=1578412+-+Interleukin+Inhibitors+Global+Markets+Report+2020-2030%3a+Focus+on+IL-17%2c+IL-23%2c+IL-1%2c+IL-5%2c+IL-6&utm_exec=chdo54prd

32. Global Interleukin Inhibitors Market: By Type: L-17, IL-23, IL-1, IL-5, IL-6, Others; By Application: Psoriasis, Psoriatic Arthritis, Rheumatoid Arthritis, Asthma, Inflammatory Bowel Disease, Others; Regional Analysis; Historical Market and Forecast (2016-2026); SWOT Analysis; Competitive Landscape; Industry Events and Developments. EMR. Retrieved August 24 2021 from: https://www.expertmarketresearch.com/reports/interleukin-inhibitors-market

33. Hidradenitis suppurativa: Diagnosis and treatment. The American Academy of Dermatology Association. Retrieved August 24 2021 from: https://www.aad.org/public/diseases/a-z/hidradenitis-suppurativa-treatment

34. Blanco, Ricardo et al. Long-term Successful Adalimumab Therapy in Severe Hidradenitis Suppurativa. Archives of dermatology, 2019; 145(5): 580-584. https://doi.org/10.1001/archdermatol.2009.49

35. Global hidradenitis suppurativa market set to reach $1.81bn by 2028. Global Data. September 17 2019. Retrieved August 24 2021 from: https://www.globaldata.com/global-hidradenitis-suppurativa-market-set-to-reach-1-81bn-by-2028/

36. Global Atopic Eczema Treatment market Will Reach USD 34,089.3 Million by 2026: Facts & Factors. Intrado. April 07 2021. Retrieved August 24 2021 from: https://www.globenewswire.com/en/news-release/2021/04/07/2205772/0/en/Global-Atopic-Eczema-Treatment-Market-Will-Reach-USD-34-089-3-Million-by-2026-Facts-Factors.html

37. Global Atopic Dermatitis Treatment Market Size, Share, Trends, COVID-19 Impact & Growth Analysis Report - Segmented By Treatment Type, Route Of Administration, Distribution Channel & Region - Industry Growth, Trends & Forecast (2021 to 2026). Market Data Forecast. April 2021. Retrieved August 24 2021 from: https://www.marketdataforecast.com/market-reports/atopic-dermatitis-treatment-market

38. Biologics 101. HMP Global Learning Network. February 2012. Retrieved August 27 2021 from: https://www.hmpgloballearningnetwork.com/site/thederm/site/cathlab/event/biologics-101

39. Iffat, Hassan et al. Biologics in Dermatology: A Brief Review. British Journal of Medical Practitioners. December 2013, 6(4): a629.

40. Virtual Clinical Trials: The Future of Dermatology Studies. Contractpharma. Retrieved August 27 2021 from: https://www.contractpharma.com/contents/view_experts-opinion/2021-01-15/virtual-clinical-trials-the-future-of-dermatology-studies/

41. Clinical Trials.gov. U. S. National Library of Medicine. Retrieved September 30 2021 from: https://clinicaltrials.gov/ct2/home

42. Elsie, Grace et al. Injection Site Reaction in the Federal Adverse Event Reporting System (FAERS) Post-Marketing Database Vary Among Biologics Approved to Treat Moderate-to-Severe Psoriasis. Dermatology and Therapy. November 16 2019, 10: 99-106.

43. Shanthi, Narla et al. The most recent advances in understanding and managing hidradenitis suppurativa. F1000Res. August 26 2020. https://doi.org/10.12688/f1000research.26083.1

44. Thenaporn, Ratchataswan et al. Biologics for Treatment of Atopic Dermatitis: Current Status and Future Prospect. The Journal of Allergy and Clinical Immunology: In Practice. March 2021, 9(3): 1053-1065. https://doi.org/10.1016/j.jaip.2020.11.034

45. Jodi L., Johnson. Biologics are Changing the Landscape of Eczema Treatment. National Eczema Association. June 3 2021. Retrieved August 24 2021 from: https://nationaleczema.org/biologics-eczema-treatment/

46. Abbott Announces 10-Year data Evaluating Humira® (Adalimumab) for patients with Long-Standing Moderate-to-Severe Rheumatoid Arthritis. Abbott. June 6 2012. Retrieved August 24 2021 from: https://abbott.mediaroom.com/2012-06-05-Abbott-Announces-10-Year-Data-Evaluating-HUMIRA-Adalimumab-for-Patients-with-Long-Standing-Moderate-to-Severe-Rheumatoid-Arthritis

47. Structure and Content of Clinical Study Reports. European Medicines Agency. July 1996. Retrieved August 30 2021 from: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-3-structure-content-clinical-study-reports-step-5_en.pdf

48. Botox Injections. Mayo Clinic. February 2 2021. Retrieved April 28 2021 from: https://www.mayoclinic.org/tests-procedures/botox/about/pac-20384658#:~:text=Botox%20injections%20are%20noted%20primarilyalso%20help%20prevent%20chronic%20migraines

49. Facial Injectable Market Growth & Trends. Grand View Research. Retrieved April 20 2021 from: https://www.grandviewresearch.com/press-release/global-facial-injectables-market

50. Van Dyke et al. Severe Acute Local Reactions to a Hyaluronic Acid-derived Dermal Filler. The Journal of Clinical and Aesthetic Dermatology. May 2010. 3(5): 32–35.

51. Regulation (EU) 2017/745 of the European Parliament and of the Council. Official Journal of the European Union. April 5 2017. Retrieved April 20 2021 from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745

52. The Global Facial Injectable Market. Market Research Future. Retrieved April 20 2021 from: https:// www.marketresearchfuture.com/reports/facial-injectable-market-1527

53. Facial Injectable Market Growth & Trends. Grand View Research. Retrieved April 20 2021 from:

https://www.grandviewresearch.com/press-release/global-facial-injectables-market

54. Plastic Surgery Statistics Report. American Society of Plastic Surgeons. 2019. Retrieved April 20 2021 from: https://www.plasticsurgery.org/documents/News/Statistics/2019/plastic-surgery-statistics- full-report-2019.pdf

55. Highlights of Prescribing Information. Allergan. June 26 2019. Retrieved April 20 2021 from: https:// media.allergan.com/actavis/actavis/media/allergan-pdf-documents/product-prescribing/20190626- BOTOX-Cosmetic-Insert-72715US10-Med-Guide-v2-0MG1145.pdf

56. Christiansen, Lauren. How Fenty's brand positioning generated $100 million in its first 40 days. Jilt. March 19 2021. Retrieved April 20 2021 from: https://jilt.com/blog/fenty-brand-positioning/

57. ExpertInSkinAndHairTypesAroundTheWorld.L'Oréal.RetrievedApril202021from: https://www.loreal.com/en/articles/science-and-technology/expert-inskin/

58. Amerson, Erin et al. Cutaneous Reactions Reported after Moderna and Pfizer COVID-19 Vaccination: A Registry-Based Study of 414 Cases. Journal of the American Academy of Dermatology. March 26 2021. https://doi.org/10.1016/j.jaad.2021.03.092

59. Remote Patient Monitoring will Continue to Transform Healthcare Delivery and Clinical Trials in 2021. GlobalData. January 19 2021. Retrieved April 20 2021 from: https://www.globaldata.com/ remote-patient-monitoring-will-continue-transform-healthcare-delivery-clinical-trials-2021/

60. Negreiro, Mar. The Rise of Digital Health Technologies During the Pandemic. European Parliamentary Research Service. April 2021. Retrieved April 28 2021 from: https:// www.europarl.europa.eu/RegData/etudes/BRIE/2021/690548/EPRS_BRI(2021)690548_EN.pdf

61. Telemedicine to Benefit the Most from Remote Patient Monitoring Tools: Poll. Pharmaceutical Technology. January 25 2021. Retrieved April 20 2021 from: https://www.pharmaceutical- technology.com/news/telemedicine-to-benefit-the-most-from-remote-patient-monitoring-tools-poll/

62. Expansion of Telehealth During COVID-19 Pandemic. Epic Health Research Network. May 5 2020. Retrieved April 20 2021 from: https://www.ehrn.org/articles/expansion-of-telehealth-during-covid-19-pandemic/

63. Balfour, Hannah. COVID's Impact on Cancer Therapeutics: Clinical Trial and Treatment Disruptions. European Pharmaceutical Review. February 19 2021. Retrieved April 20 2021 from: https://www.europeanpharmaceuticalreview.com/article/143162/covids-impact-on-cancer- therapeutics-clinical-trial-and-treatment-disruptions/

64. Balfour, Hannah. COVID's Impact on Cancer Therapeutics: Clinical Trial and Treatment Disruptions. European Pharmaceutical Review. February 19 2021. Retrieved April 20 2021 from: https://www.europeanpharmaceuticalreview.com/article/143162/covids-impact-on-cancer-therapeutics-clinical-trial-and-treatment-disruptions/

65. Poll suggests trial protocol should be changed for remote monitoring. Clinical Trials Arena. March 30 2021. Retrieved April 20 2021 from: https://www.clinicaltrialsarena.com/news/poll-suggests-trial-protocol-should-be-changed-for-remote-monitoring/

66. Telehealth, Remote Patient Monitoring Crucial to Long-Term Cardiac Health Implications of COVID-19. EP Lab Digest. July 6 2020. Retrieved April 20 2021 from: https://www.eplabdigest.com/telehealth-remote-patient-monitoring-crucial-long-term-cardiac-health-implications-covid-19

67. Telehealth, Remote Patient Monitoring Crucial to Long-Term Cardiac Health Implications of COVID-19. EP Lab Digest. July 6 2020. Retrieved April 20 2021 from: https://www.eplabdigest.com/telehealth-remote-patient-monitoring-crucial-long-term-cardiac-health-implications-covid-19

68. COVID Research Updates: Older People are at Higher Risk of Getting COVID Twice. Nature. March 19 2021. Retrieved April 20 2021 from: https://www.nature.com/articles/d41586-020-00502-w

69. Allen, Arthur. Kids Should be Part of COVID Vaccine Trials, Pediatricians Say. Kaiser Health News. December 16 2020. Retrieved April 20 2021 from: https://www.masslive.com/coronavirus/2020/12/kids-should-be-part-of-covid-vaccine-trials-pediatricians-say.html

70. Blumenthal Kimberly et al. Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS CoV-2. The New England Journal of Medicine. April 1 2021. Retrieved April 20 2021 from: https://www.nejm.org/doi/full/10.1056/NEJMc2102131

71. Fact check: It is Standard Practice for Vaccine Safety Monitoring to Continue after Approval. Reuters. February 13 2021. Retrieved April 20 2021 from: https://www.reuters.com/article/uk- fact-check-vaccine-monitoring-idUSKBN2AC2G3

72. Plana, Deborah et al. Re-Envisioning Clinical Trials During The COVID-19 Pandemic. Health Affairs Blog. July 8 2020. Retrieved April 20 2021 from: https://www.healthaffairs.org/do/10.1377/hblog20200702.963588/full/

73. Haque, Waqas et al. Lack of Diversity in Clinical Trials: The Problem and Potential Solutions. Hopkins Biotech Network. November 20 2020. Retrieved April 20 2020 from: https://hopkinsbio.org/academic/diversity-in-clinical-trials/

74. Corr, Peter et al. The Pathway from Idea to Regulatory Approval: Examples for Drug Development. National Academy of Sciences: Conflict of Interest in Medical Research, Education, and Practice. 2009. COVID-19: Research, products and services in Austria. LISAvienna. Retrieved April 20 2021 from: https://www.lisavienna.at/life-sciences-in-vienna/covid-19/#c1101

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