

## **Measures against illegal offers of fresh cell therapy and non-approved fresh cell products**

Federal Office of Public Health (FOPH) and Swiss Agency for Therapeutic Products (Swissmedic)

Fresh cell therapy continues to be offered in Switzerland and is heavily advertised on the Internet. Medical tourists from Asia are the main customers; these products have considerable commercial significance. However, the efficacy of fresh cell therapies is not scientifically proven and they are associated with substantial health risks. Several offers are outside the legal framework or illegal, and therefore represent also a reputational risk for Switzerland. The FOPH and Swissmedic have worked closely with the cantonal authorities to prepare an overview of existing treatment offerings. Potential producers of fresh cells and fresh cell products, as well as suppliers of treatments using these products, are referred to the relevant legislation and are required to cease any manufacture or treatment that has not received the necessary authorisations or permits, to refrain from advertising these, and to submit appropriate applications.

### **INTRODUCTION**

Fresh cell therapy is a treatment regimen that is not currently accepted by medical science, but is very popular with wealthy customers participating in medical tourism in Switzerland. Fresh cell therapy was originally developed around 1930 by the Swiss doctor Paul Niehans (1882-1971), and involved the suspension of live animal cells in an isotonic saline solution and their subsequent transfer to patients. The cell material is derived from animal organs, usually from the organs of sheep fetuses or from sheep placentas. There is now an increasing trend towards the use of frozen or lyophilised cells, cell fragments or cell extracts instead of living cells. The therapy essentially involves the injection of such extracts with the purpose of revitalizing the corresponding organs. This procedure is often performed in the context of anti-aging therapies or therapies aimed at general revitalization of the body. However, treatments are also offered that range from therapies for chronic diseases and afflictions of the elderly (e.g. migraines, atherosclerosis etc.) through to alternative cancer treatments.

Fresh cell therapy is often advertised (usually on the websites of clinics and practices) as 'cell therapy' or even 'treatment with stem cells'. Treatments that involve products that stimulate the immune system are also intentionally represented as being associated with fresh cell therapy in order to build on the reputation of the treatment originally developed by Niehans. In these advertisements there is therefore no clear distinction between the terms used, so that it is difficult for the layman to differentiate clearly between fresh cell therapy and new scientific techniques of cell therapy (such as treatments with stem cells) that are currently being developed.

### **The risks of fresh cell therapy**

The efficacy of fresh cell therapy has not been scientifically proven. The lack of therapeutic benefits must be weighed up against the significant health risks. In particular, these risks include hypersensitivity reactions, abscess formation through to sepsis at the injection site, infection with zoonotic agents (microorganisms that occur in vertebrates and can be transmitted to humans), as well as induction of autoimmune diseases such as rheumatism. There have even been some fatalities after treatment with fresh cells (1-5). The therapy is therefore rejected by professional medical associations and the WHO (6-8).

There have been various reasons for official prohibition of the treatment, primarily on the grounds of safety. Such an attempt was made by the Federal Government in Germany in 1997 and failed three years later in the Federal Constitutional Court, but only for formal reasons (9).

## Situation in Switzerland

Fresh cell therapy and related treatments are becoming increasingly popular, particularly with people from China, Russia and the Middle East. Accurate figures on the use of such therapies in Switzerland are not available. However, in 2011 a total of 913 visas for medical treatment in Switzerland were issued in China alone. However, these visas provide no detailed information on the type of treatment. It is estimated that about 80% of these, or about 730 treatments per year, were related to the provision of such treatments.

Since the cantons are responsible for medical activities in clinics or practices, the FOPH and Swissmedic do not have comprehensive information on fresh cell therapy offerings in Switzerland. However, it is clear that the number of these offerings is increasing, especially on the websites of various clinics, practices and medical personnel in Switzerland. At the same time, there has been a significant increase in enquiries by potential and also anxious customers in connection with fresh cell therapies and similar treatments with regard to approved clinics as well as authorised treatments and products.

So far, neither the FOPH nor Swissmedic has issued any authorisations, manufacturing permits or any other approvals for products used in fresh cell therapy or their application. It is possible that certain therapies that are currently offered are outside the legal framework and therefore not permissible.

In addition to the health risks outlined above for people seeking fresh cell therapy, there is also a significant reputational risk for Switzerland. The use of highly controversial therapies that have not received the necessary regulatory authorisations or permits could result in lasting damage to Switzerland's reputation as a supplier and exporter of high-quality health services.

## THE LEGAL FRAMEWORK IN SWITZERLAND

Different legal frameworks apply to treatment with live animal cells (xenotransplantation) and treatment with cell fragments or cell extracts of animal origin (classified as medicinal products), and these differences must be taken into account. Activities or use of fresh cell therapy or products, as well as other cell-based products of human or animal origin, are subject in particular to the following legal provisions:

- **Fresh cell therapy with live animal cells** is a xenotransplantation and is subject to the Federal Act of 8 October 2004 on the Transplantation of Organs, Tissues and Cells (Transplantation Act; SR 810.21). Xenotransplantation requires an authorisation from the FOPH. Granting of this authorisation is subject to strict requirements in order to exclude or minimise the risk of transmitting pathogens from animals to humans. The transplantation of human cells, tissues and organs is also subject to the Transplantation Act, which provides for appropriate authorisations from the FOPH.
- Novel types of cell therapy in which products from cells, tissues or organs are produced, referred to as **transplant products**, are subject to the Transplantation Act and the Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (Therapeutic Products Act, TPA; SR 812.21). This results in various licensing and marketing authorisation requirements for transplant products and their preparation in order to ensure their safety, efficacy and quality.
- The Transplantation Act does not apply to **cell extracts (without live cells) of human or animal origin**. These preparations are classified as medicinal products and are subject to the Therapeutic Products Act. Until 2010, these products for fresh cell therapy could be classified as '*magistral formulas*' (for filling a medical prescription), which exempted them from the marketing authorisation otherwise required by the TPA. As '*magistral formula*' medicinal

products, these preparations were under the jurisdiction of the respective canton. With the amendment of the Therapeutic Products Act on 1 October 2010, classification of these products as *magistral formulas* is no longer possible, since the cell extracts or fragments used cannot be classified as authorised active substances according to Art. 19d of the Ordinance of 17 October 2001 on medicinal products (Ordinance on Medicinal Products, VAM; SR 812.212.21). For this reason, since then such preparations have been subject to the requirement for marketing authorisation according to Art. 9, para. 1 of the TPA. Marketing authorisation can be granted if the requirements regarding quality, safety and efficacy are met. The manufacture and distribution of such products require a license from Swissmedic. This also applies to their **import, wholesale and export.**

- If certain patients need a particular **medicinal product** that is **not authorised** in Switzerland, its **import** by a health professional requires a permit from Swissmedic for a particular case (Art. 36 Ordinance concerning Authorisations for Medicinal Products, AMBV; SR 812.212.1).
- Given the nature and origin of the starting material as well as the type of application (frequently injection), it is not possible to classify products for fresh cell therapy as **cosmetics** or, if administered orally, as **dietary supplements.**
- The **supervision and control of medical activities in clinics, practices and of medical personnel** who provide or use such treatments continue to be the responsibility of the relevant enforcement agencies of the cantons.
- **Public advertising** of the above-mentioned treatments is subject to national and cantonal legislation on the practice of medicine. Advertising of treatments with transplant products or preparations containing cell extracts must also comply with the requirements of the Ordinance of 17 October 2001 on the advertising of medicinal products (Ordinance on Advertising Medicinal Products, AWV; SR 812.212.5). This applies particularly to the advertising of such treatments on the Internet.
- For the **harvesting of fresh cells from animal fetuses or animal organs**, the provisions of the Animal Welfare Act of 16 December 2005 (Tierschutzgesetz; SR 455) and the Animal Protection Ordinance of 23 April 2008 (Tierschutzverordnung; SR 455.1) must be observed. The Federal Food Safety and Veterinary Office (FSVO) is responsible for these legal issues. The killing of animals that are not to be used as food is classified under animal experimentation and requires an appropriate permit.

## MEASURES AGAINST THE OFFERS OF ILLEGAL TREATMENTS

Concerns regarding possible health risks for patients, reputational risks for Switzerland and the fragmented and limited nature of cantonal enforcement have prompted various federal authorities (Federal Department of Foreign Affairs FDFA, State Secretariat for Economic Affairs SECO, FOPH and Swissmedic) to address the problem of illegal supply of fresh cell therapy in Switzerland together with the cantonal authorities.

### Action plan

Under the auspices of the FOPH and Swissmedic, a plan for measures was developed in close collaboration with the Conference of Cantonal Ministers of Public Health (GDK), the Association of Cantonal Pharmacists (KAV) and the Swiss Association of Cantonal Officers of Health (VKS) with the following objectives:

1. An overview of the offerings and products used in clinics and practices should improve transparency and clarify how the applicable legislation is to be enforced;
2. The illegal manufacture and use of fresh cell therapy in Switzerland is to be permanently prohibited;
3. The offering and application of fresh cell therapy is only permissible if the products have been authorised as medicinal products by Swissmedic or their use as transplants has been approved by the FOPH.

The cantons, the FOPH and Swissmedic collaborate on these measures according to their respective areas of responsibility.

## Information collection

In the summer of 2014, all cantons prepared an inventory on behalf of the FOPH and Swissmedic of the known or suspected suppliers (clinics, practices and medical personnel) of fresh cell therapy as well as manufacturers of fresh cells and fresh cell products. In the autumn of 2014, the cantons carried out the next step, which involved collection of the information required from the clinics to clarify whether these offerings were legal or illegal. The cantons were provided with a consistent and detailed questionnaire for this purpose. By late November, a series of self-declarations of potential manufacturers and suppliers of fresh cell therapies had been received.

These self-declarations were assessed by Swissmedic and the FOPH. Both agencies worked closely together and coordinated the steps with the cantons concerned. The actions of Swissmedic and the FOPH are confined to offerings and activities that are covered by the TPA and/or the Transplantation Act, as well as the relevant requirements for marketing authorisations and licenses. Where indicated, it will be clarified with the cantons as to whether cantonal authorisations were issued according to the superseded Act (before revision of the TPA in 2010). The oversight on medical use (illegal applications, breach of duty of care) is still the responsibility of the cantons. Contacts with suppliers are made in consultation with the canton.

Suspected violations on other legal grounds are forwarded to the appropriate authorities. The focus is still on offerings in Switzerland.

## Results

Based on research by the cantons, an initial inventory of a total of 35 institutions or individuals was prepared, for which offerings of fresh cell therapy in any form (or similar treatments) were suspected. These providers were distributed among three cantons. The institutions that were identified were requested by the cantons to declare any activities relating to fresh cells with the aid of a detailed questionnaire. It is assumed that this inventory is incomplete, and that additional institutions (also in other cantons) advertise such offerings.

Analysis of the declarations showed that none of these institutions perform fresh cell therapy in the original sense of the term, i.e. no live animal cells or tissues are administered with any of the treatments. However, preparations manufactured from animal cells or tissues are used in some institutions. These preparations are very heterogeneous:

- Lyophilised and frozen extracts from animal organs and fetuses, processed by centrifugation in some cases;
- Organ lysates or homogenates;
- Homeopathic dilutions of animal or human material.

Administration of these preparations is predominantly parenteral (injection), but also oral. Although individual manufacturers were reported from two cantons, the preparations used are usually not authorised in Switzerland and are imported into Switzerland from France or Germany by medical personnel.

Some of the reported offerings involve the use of preparations that are subject to the Therapeutic Products Act and therefore to enforcement by Swissmedic and the cantons. Certain other preparations are subject to the Transplantation Act and are therefore the responsibility of the FOPH.

In the evaluation of these reports, special attention was paid to the information provided by the websites of the institutions. There were often discrepancies between the information given by the clinics on their websites and that declared in their reports. It is assumed that the terms "fresh cells" or "cell therapy" are often intended to imply an association with the earlier forms of fresh cell therapy originated by Niehans, even though these treatments are no longer carried out. The institutions concerned are being requested

to correct their published information.

Evaluation of the declarations received has shown that the institutions can be roughly divided into four different groups:

1. Eighteen institutions declared that they did not engage in any activities with fresh cells, fresh cell preparations or other cell-based products.  
For this group, the information on the websites was checked and clarified with the cantonal authorities. In some cases, objections to the information displayed on the website have already been raised.
2. Six institutions declared that they did not engage in any activities with fresh cells or fresh cell preparations, but they reported activities with "stem cells" or adipose tissue.  
For this group, the information on the websites was checked and the institutions were requested to comply with the legal requirements applicable to transplants and transplant products according to the Transplantation Act, and to obtain any necessary authorisations and/or licenses from the FOPH and/or Swissmedic for activities with transplants or transplant products.
3. Five institutions had declared that they import fresh cell preparations or other medicinal products via medical personnel and use them in Switzerland.  
If these imported preparations are not authorised in Switzerland, they are subject to the provisions of Art. 36 AMBV (Ordinance concerning Authorisations for Medicinal Products) and require special permits. Art. 36 AMBV allows the import of unauthorised finished medicinal products under certain conditions relating to the importing person, the purpose and the marketing authorisation status of the product in the exporting country. The institutions concerned have been requested to submit the necessary documents or obtain permits for importation of the unauthorised medicinal products.
4. Six institutions declared having own manufacturing activities.  
For these institutions, the precise manufacturing arrangements (contract or autonomous manufacturers) will be checked in the course of further investigations and the necessary measures taken.

## Further procedure

All providers who completed the questionnaire receive a report from the responsible authority for their information, with an assessment of the declaration and references to the applicable legislation relating to manufacture, distribution, use and promotion and, depending on the findings, an injunction to cease activities that are not lawfully authorised or submit the necessary applications for authorisation or a license to Swissmedic or the FOPH.

Swissmedic (responsible for manufacturers and distributors of medicinal products), the FOPH (responsible for offerings with cells and tissues) and the cantonal authorities (responsible for the use of such products) check clinics, practices and medical personnel for compliance with the applicable legislation using a risk-based approach. It is likely that there are other providers that were not recorded in the inventory. These are hereby requested to review their treatment offerings and other activities with fresh cell preparations for their conformity with the law and, where appropriate, to obtain the necessary licenses and authorisations in accordance with the legal framework described above.

For the information of interested customers and to reduce the reputational risk for Switzerland as a supplier of medical services, information on fresh cell therapy together with its risks and the relevant legislation will be posted on the websites of the FOPH and Swissmedic. This information will also be publicised in an appropriate form in the countries from which the majority of medical tourists in Switzerland originate.

## Contact

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## Further information

Federal Act on the Transplantation of Organs, Tissues and Cells (Transplantation Act):  
[http://www.admin.ch/ch/e/rs/810\\_21/index.html](http://www.admin.ch/ch/e/rs/810_21/index.html)

Federal Law on Medicinal Products and Medical Devices (Therapeutic Products Act, TPA):  
<http://www.admin.ch/opc/en/classified-compilation/20002716/index.html>

Verordnung über die Arzneimittel (VAM [Ordinance on Medicinal Products]):  
[www.admin.ch/opc/de/classified-compilation/20011787/index.html](http://www.admin.ch/opc/de/classified-compilation/20011787/index.html)

Verordnung über die Bewilligungen im Arzneimittelbereich (AMBV [Ordinance concerning Authorisations for Medicinal Products]):  
[www.admin.ch/opc/de/classified-compilation/20011780/index.html](http://www.admin.ch/opc/de/classified-compilation/20011780/index.html)

Verordnung über die Arzneimittelwerbung (AWV [Ordinance on Advertising Medicinal Products]):  
[www.admin.ch/opc/de/classified-compilation/20011778/index.html](http://www.admin.ch/opc/de/classified-compilation/20011778/index.html)

Tierschutzgesetz (TSchG [Animal Protection Act]):  
[www.admin.ch/opc/de/classified-compilation/20022103/index.html](http://www.admin.ch/opc/de/classified-compilation/20022103/index.html)

Tierschutzverordnung (TSchV [Animal Protection Ordinance]):  
[www.admin.ch/opc/de/classified-compilation/20080796/index.html](http://www.admin.ch/opc/de/classified-compilation/20080796/index.html)

[www.bag.admin.ch](http://www.bag.admin.ch) / English / Topics / Diseases and medicine / Therapeutic products / Topics / Fresh Cell Therapy

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6. Mit Stammzellen heilen: Was heute möglich ist. Und was nicht [*Healing with stem cells: What is possible today, and what is not*]. Data sheet of the NRP (National Research Programme) 63 - Stem

Cells and Regenerative Medicine

(available at: [http://www.nfp63.ch/SiteCollectionDocuments/nfp63\\_merkblatt\\_stammzellen\\_d.pdf](http://www.nfp63.ch/SiteCollectionDocuments/nfp63_merkblatt_stammzellen_d.pdf))

7. Warning of the American Cancer Society (available at: <http://www.cancer.org/treatment/treatmentsandsideeffects/complementaryandalternativemedicine/pharmacologicalandbiologicaltreatment/cell-therapy>)
8. Statement of the WHO on xenotransplantation (available at: <http://www.who.int/transplantation/XenoEnglish.pdf>)
9. Prohibition of fresh cell production is invalid. The Confederation had no regulatory powers. Press release no. 18/2000 of 16 February 2000 of the Federal Constitutional Court on Judgement 1BvR 420/97 (available in German at: <http://www.bundesverfassungsgericht.de/SharedDocs/Pressemitteilungen/DE/2000/bvg00-018.html>)