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THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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Thin Film Polycaprolactone Device Implant

Based on public information

Developer(s)

University of California

Originator

https://www.universityofcalifornia.edu/

United States

The University of California (UC) was founded in 1868 with the establishment of its first campus, UC Berkeley. Over the years, it has grown into a leading public university system with a strong emphasis on research and innovation. UC has been at the forefront of numerous scientific and pharmaceutical technological advancements in alliance with external collaborators.

Sponsor(s)

No sponsor indicated

Partnerships

RTI International
https://www.rti.org/

U.S. Agency for International Development (USAID)
https://www.usaid.gov/

United States President's Emergency Plan For AIDS Relief (PEPFAR)
https://www.hiv.gov/federal-response/pepfar-global-aids/pepfar

Magee-Womens Research Institute & Foundation
https://mageewomens.org/

Technology information

Type of technology

Polymer-based particles

Administration route

Subcutaneous, Intra-vitreal

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Rilpivirine (RPV)

Development Stage

Pre-clinical

Regulatory Approval

Not provided

Description

Thin Film Polycaprolactone Devices (TFPDs) are novel, biodegradable platforms designed for subcutaneous or ocular administration, capable of sustained release of both small and large molecules. By manipulating the polycaprolactone (PCL) polymer's degradation profile, fabrication parameters, and characterization. TFPDs can be tailored to achieve desired pharmacokinetic profiles for a wide range of APIs. This technology has the potential to deliver a linear release rate for up to three months.

Technology highlight

• Biodegradable material • Suitable for subcutaneous and ocular administration • Customizable release rate, duration, and storage stability • Minimal invasive application (no sutures or anesthesia required)

Technology main components

1) Multilayer of different variations of Polycaprolactone (PCL) membranes 2) Polymers: Polyethylene glycols, cyclodextrins, polysorbates, and co-polymers such as poloxamers 3) Stabilizers 4) Preservatives including Antioxidants 5) Release Modifiers 6) PDMS (Polydimethylsiloxane) annulus 7) Dyes 8) Emulsifiers 9) Other additives are added based on API's physicochemical properties such as inert fillers, anti-irritants, gelling agents, surfactants, emollients, coloring agents, buffering agent 10) Pore-forming agent (eg: Gelatin)

Information on the raw materials sourcing, availability and anticipated price

Not provided

Delivery device(s)

Thin Layer Polycaprolactone Device

APIs compatibility profile

API desired features

Water-soluble molecules

Water-insoluble molecules

Small molecules

The target compounds encompass a broad spectrum of therapeutic classes, including immunosuppressants such as methotrexate, antiglaucoma, anti-inflammatory, immunosuppressant, vitamin, micronutrient, antioxidant, antibacterial (e.g., vancomycin, cephazolin), antiviral (e.g., ganciclovir, acyclovir, foscarnet), antifungals (e.g., amphotericin B, fluconazole, voriconazole), anticancer agents (e.g., cyclophosphamide, melphalan), vitamins, zinc, copper and zeaxanthin.

Proteins

TFPD system is developed for a range of therapeutic proteins, including: VEGF inhibitors, hematopoietic factors such as erythropoietin, thrombolytic agents like tissue plasminogen activator, collagenolytic enzymes like hyaluronidase and microplasmin, immunomodulatory agents such as etanercept, infliximab, and daclizumab, neuromuscular agents like botulinum toxin A, complement inhibitors targeting the C3 component, antibody therapeutics including ranibizumab, bevacizumab, trastuzumab and other molecules such as insulin, interferon alpha-2b.

Additional solubility data

Not provided

Additional stability data

The stability of the API within the TFPD device reservoir was assessed, devices containing residual API were opened, and the contents were dissolved in a release buffer. The API purity was then quantified using reverse-phase high-performance liquid chromatography (RP-HPLC). This analytical method effectively separates the API from process impurities and degradation products generated during the manufacturing process. The results demonstrated that the API purity remained consistent within the device reservoir for up to 49 days of storage. However, a significant decrease of 19% in API purity.

API loading: Maximum drug quantity to be loaded

75-90 wt%

API co-administration

1 single API : i

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

The fabrication of the TFPD system utilized two primary pieces of equipment: a circular mold and a laser beam. Other equipments were not disclosed.

Manufacturing

Fabrication of the TFPD involves a few steps that include 1)Spin casting PCL +Gelatin onto a flat circular mold 2)A mixture of polycaprolactone (PCL) and gelatin is spin-cast onto the mold to form a uniform polymer layer. 3)A drug pellet or solution is applied to the bioagent layer positioned between two PCL layers. 4)The assembled layers are dried using either an evaporation or lyophilization technique. 5)A heated PDMS annulus is applied to seal the polymer layers at 80°C. 6)The sealed device is subjected to lyophilization to remove moisture. 7) At last Zinc oxide nanowire rod is integrated.

Specific analytical instrument required for characterization of formulation

1) Scanning Electron Microscope 2) XP - 2 Stylus Profiler 3) SpectraMax 190 microplate reader

Clinical trials

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Biodegradable
- Drug-eluting
- Monolithic
- Room temperature storage

Release properties

The release rate (constant) of the API is tunable based on the characteristics of the targeted API. In TFPD, the dissolved drug is driven by a concentration gradient between the drug-laden reservoir and the external environment and partitions into the polymeric membrane. Subsequently, the drug diffuses through the membrane and into the surrounding bulk fluid. Preclinical studies of tenofovir show that the API undergoes a linear release rate ranging from 0.5 to 4.4 mg/day for 60-90 days.

Injectability

TFPD administration involves a minor surgical procedure and non injectable. The device is inserted into the subcutaneous tissue via a small incision made in the skin.

Safety

Safety studies in humans are yet to be conducted.

Stability

Stability studies conducted on TFPD devices loaded with API demonstrated that the purity of the API remained unchanged within the device reservoir for a storage period of up to 49 days.

Storage conditions and cold-chain related features

TFPD is customizable to an acceptable storage condition depending on the indication and target patient population.

Potential application(s)

Therapeutic area(s)

HIV

Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Use of technology

Ease of administration

- Administered by a community health worker
- Administered by a nurse
- Administered by a specialty health worker

Frequency of administration

Weekly, Monthly

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults
- Older Adults

Genders

- All

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

Unspecified

Comment

Not provided

Potential associated API(s)

Elvitegravir (EVG)

Class(es)

Antiretroviral agent

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

HIV

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Rilpivirine (RPV)

Class(es)

Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

HIV

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Tenofovir alafenamide (TAF)

Class(es)

Nucleoside reverse transcriptase inhibitors (NRTIs)

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Description

Multilayer Thin Film drug delivery Device and Methods of making and using the same

Brief description

Multilayer thin film devices that include a bioactive agent for elution to the surrounding tissue upon administration to a subject are provided. The multilayer thin film devices are useful as medical devices, such as ocular devices. Also provided are methods and kits for localized delivery of a bioactive agent to a tissue of a subject, and methods of preparing the subject devices. The multilayer thin film medical device includes a first layer, a bioactive agent, and a second layer. The first and the second layers may be porous or non-porous. The devices have a furled structure, suitable for administration to a subject.

Representative patent

US11185499B2

Category

Device

Patent holder

The Regents of the University of California

Exclusivity

Not provided

Expiration date

April 12, 2032

Status

Not provided

Supporting material

Publications

** Schlesinger, E., Ciaccio, N., & Desai, T. A. (2015). Polycaprolactone thin-film drug delivery systems: Empirical and predictive models for device design. Materials science & engineering. C, Materials for biological applications, 57, 232–239. https://doi.org/10.1016/j.msec.2015.07.027 **

To define empirical models and parameters based on theoretical equations to describe drug release profiles from two polycaprolactone thin-film drug delivery systems. Additionally, to develop a predictive model for empirical parameters based on drugs' physicochemical properties. Release profiles from a selection of drugs representing the standard pharmaceutical space in both polycaprolactone matrix and reservoir systems were determined experimentally. The proposed models were used to calculate empirical parameters describing drug diffusion and release. Observed correlations between empirical parameters and drug properties were used to develop equations to predict parameters based on drug properties. Predictive and empirical models were evaluated in the design of three prototype devices: a levonorgestrel matrix system for on-demand locally administered contraception, a timolol-maleate reservoir system for glaucoma treatment, and a primaquine-bisphosphate reservoir system for malaria prophylaxis. Proposed empirical equations accurately fit experimental data. Experimentally derived empirical parameters show significant correlations with LogP, molecular weight, and solubility. Empirical models based on predicted parameters accurately predict experimental release data for three prototype systems, demonstrating the accuracy and utility of these models.

** Schlesinger, E. (n.d.). The Thin Film Polycaprolactone Device: A platform technology for biodegradable and tunable long-acting drug delivery**

**implants. eScholarship, University of California. https://escholarship.org/uc/item/3sp069kt#article_main **

The Thin-Film Polycaprolactone Device (TFPD) is a versatile, tunable, and biodegradable implant platform technology. It uses porous and nonporous thin-film polycaprolactone (PCL) membranes for controlled or sustained release of an API. This versatile platform applies to both ocular and subcutaneous implants. The dissertation focuses on tuning PCL degradation, fabricating PCL thin-film membranes, and designing and tuning devices for specific indications. The concepts are applied to three long-acting implant systems.

** Nyitray, C. E., Chang, R., Faleo, G., Lance, K. D., Bernards, D. A., Tang, Q., & Desai, T. A. (2015). Polycaprolactone Thin-Film Micro- and Nanoporous Cell-Encapsulation Devices. ACS nano, 9(6), 5675–5682. https://doi.org/10.1021/acsnano.5b00679 **

Cell-encapsulating devices are crucial for improving transplant success rates by advancing tissue types. To achieve this, encapsulated cells must remain viable, respond to external stimuli, and be protected from immune responses. A micro- and nanoporous thin-film cell encapsulation device from polycaprolactone (PCL) has been developed. The device allows long-term bioluminescent transfer imaging, monitoring cell viability, and device tracking. The membrane's ability to tune allows selective protection from immune cell invasion and cytokine-mediated cell death while maintaining cell function. The technology has been demonstrated in mouse models for up to 90 days, showing promise for cell encapsulation success and future immune-isolation therapies.

** Lykins, W. R., Bernards, D. A., Schlesinger, E. B., Wisniewski, K., & Desai, T. A. (2022). Tuning polycaprolactone degradation for long acting implantables. Polymer, 262, 125473. **

Polycaprolactone (PCL) is a bioresorbable polyester used in biomedical applications since the 1970s. It undergoes bulk degradation, making it ideal for drug delivery. However, the time to degradation of PCLs can be multiple years. The time to degradation is directly related to its initial molecular weight, but low molecular weight PCLs are unsuitable for implantation. A new approach involves blending low and high molecular weight polymers. The degradation rate and permeability of PCL films are insensitive to their composition, and weight-average molecular weight predicts time to fragmentation. Compositions with up to 50% low molecular weight polymer can retain high molecular weight properties, reducing time to degradation by about two-fold without sacrificing mechanical integrity.

Additional documents

- TIP program brochure by RTI International

Useful links

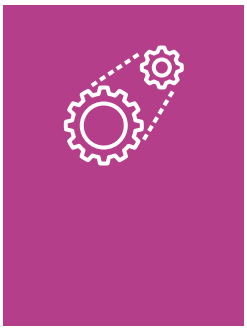
There are no additional links

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Agree



Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Agree

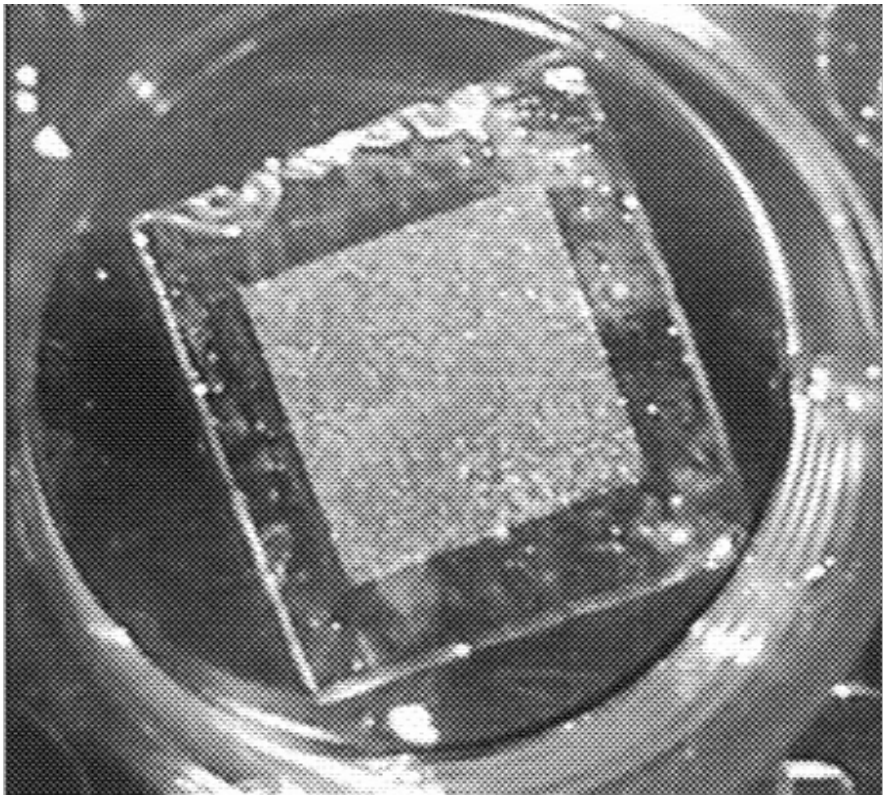
Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Agree

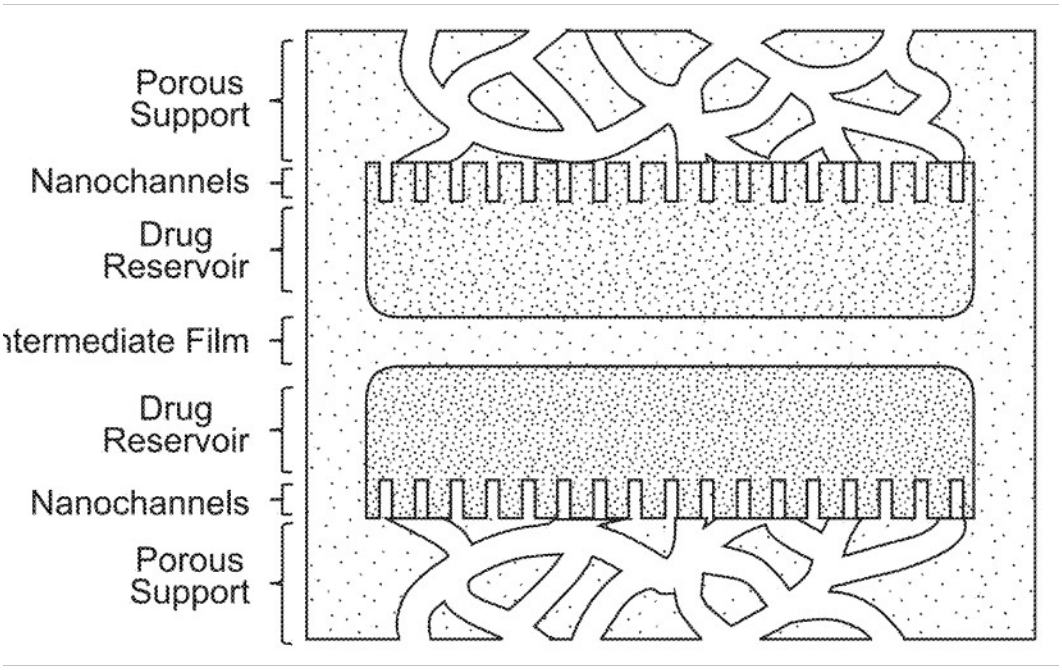
Comment & Information

Illustrations



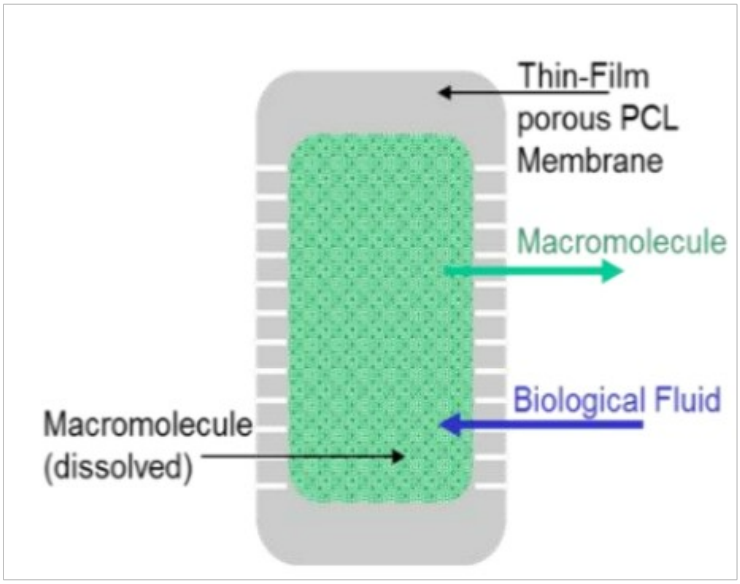
Thin Layer Polycaprolactone with an API under scanning electron microscope

U.S. Patent No. 11,185,499. (2021). United States Patent and Trademark Office. https://patentimages.storage.googleapis.com/1b/47/ea/02b5716f30411b/US11185499.pdf



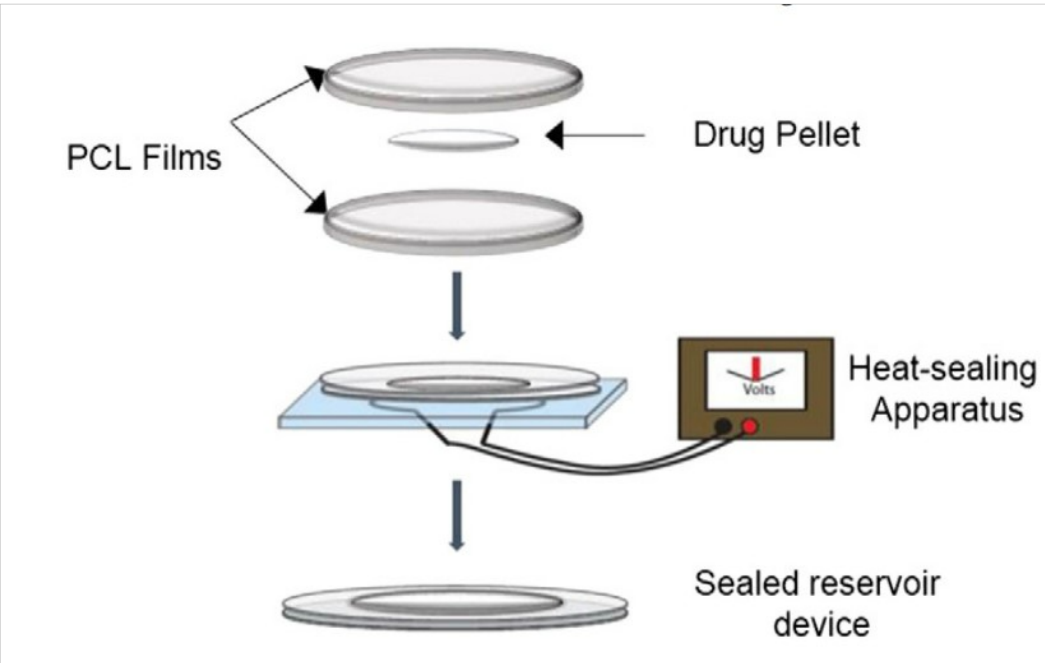
Schematic diagram of multilayer thin film device with a layer including reservoir

U.S. Patent No. 11,185,499. (2021). United States Patent and Trademark Office. https://patentimages.storage.googleapis.com/1b/47/ea/02b5716f30411b/US11185499.pdf



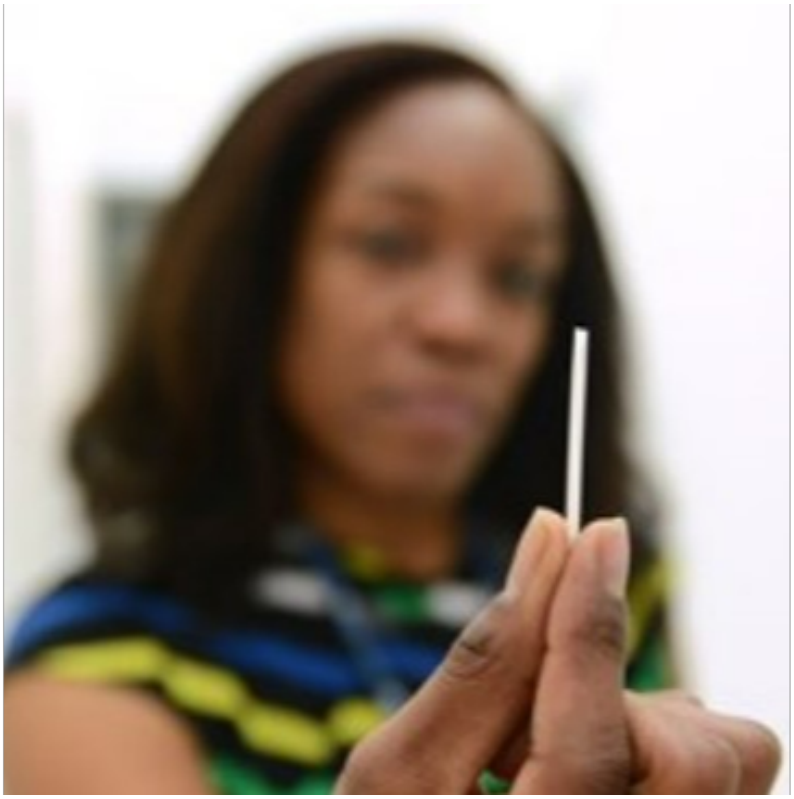
A nonporous thin film membrane controlled reservoir system in which macromolecular API is loaded as a solid into the reservoir

Schlesinger, E. B. (2015). The Thin Film Polycaprolactone Device: A platform technology for biodegradable and tunable long acting drug delivery implants. University of California, San Francisco.



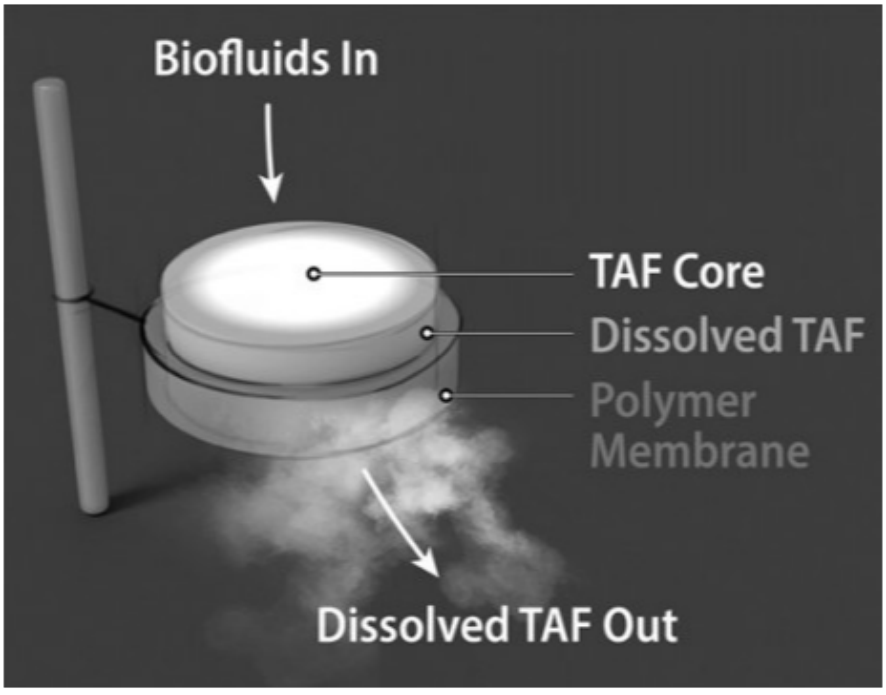
TFPD fabrication process

Schlesinger, E., Ciaccio, N., & Desai, T. A. (2015). Polycaprolactone thin-film drug delivery systems: Empirical and predictive models for device design. Materials science & engineering. C, Materials.



Thin Layer Polycaprolactone Device loaded with Tenofovir

Research Triangle Institute (RTI). (2020, November 25). TIP Program Fact Sheet [Fact sheet]. Retrieved from https://www.rti.org/sites/default/files/2020_11_25_tip_program_fact_sheet_final3.pdf



Cross Sectional view of the TFPD with Tenofovir alafenamide and its release from the polymer membrane

Research Triangle Institute (RTI). (2020, November 25). TIP Program Fact Sheet [Fact sheet]. Retrieved from https://www.rti.org/sites/default/files/2020_11_25_tip_program_fact_sheet_final3.pdf