



# safety

with injectables >



# our mission



The mission of the Physicians Coalition for Injectable Safety is to provide the public with unbiased and necessary information on injectable cosmetic treatments, appropriate injectors and where to safely access cosmetic medical procedures. Our goal is to eradicate the practice of unqualified persons providing injections, to promote treatment supervised by properly qualified and trained, board-certified doctors and to promote only the use of US FDA-approved, appropriately administered products.

The Coalition was created to provide the public with accurate, unbiased and factual information, allowing consumers to make informed choices on medical treatments. Our group represents more than 5,000 board-certified physicians across the country. Key members of the group are:

- > **American Society for Aesthetic Plastic Surgery (ASAPS)**
- > **American Academy of Facial, Plastic and Reconstructive Surgery (AAFPRS)**
- > **American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS)**
- > **American Society for Dermatologic Surgery (ASDS)**
- > **American Society of Plastic Surgeons (ASPS)**
- > **International Federation of Facial Plastic Surgery Societies (IFFPSS)**
- > **International Society of Aesthetic Plastic Surgery (ISAPS)**

For questions or concerns, please contact: [info@injectablesafety.org](mailto:info@injectablesafety.org)

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Will revise TOC  
numbering upon  
completion of revisions

Dear Colleague,

Formerly, educational initiatives by professional organizations have been directed towards technical matters of how to use injectables (fillers and neurotoxins) and the training of subordinate injectors working under the direct supervision of their physician employer.

Given the choices of cosmetic and therapeutic injectables currently approved and with more coming in each category, the question arises, “How do physicians and their staff develop processes to deliver operational excellence with injectables? This includes steps to address infection control, prevent injection errors, and maximize patient satisfaction when using injectables. While didactic education and hands-on training in the use of injectables is helpful, there has not been a substantive focus on other important parts of the process that relate to patient safety with injectables.

Medication errors occur all too frequently in patient care situations involving incorrect drug concentrations (concentrated heparin used to flush IV catheters), wrong drug (insulin mistaken for saline IV flush), and situations involving unsafe injection practices resulting in disease transmission of Hepatitis C and bacterial infections.

The Physician’s Coalition for Injectable Safety has developed a new program, *Safety With Injectables Workbook™* to provide a framework for patient safety with injectables. This program provides practitioners with a variety of templates, documents, and policies and procedures that address important components of a comprehensive process that can be developed in your clinic. This product is offered to you as a member of professional organizations that are affiliated with the Coalition.

We believe that it is important to have a great process for the safe use of injectables. The materials that are part of this offering will give you the framework for your own customized program of injectable safety. Such a program will help differentiate Core-trained injectors from others that cannot implement patient safety and quality when using injectables.

The Physician’s Coalition for Injectable Safety offers *Safety With Injectables Workbook, Second Edition™*. This edition contains updated informed consents and a chapter on the business of injectables.

Sincerely,



**Mark L. Jewell, M.D.**

Organizer, Physician’s Coalition for Injectable Safety

Past President, The American Society for Aesthetic Plastic Surgery (ASAPS)

United States National Secretary, International Society for Aesthetic Plastic Surgery (ISAPS)

# license agreement



Members in good standing of each Society affiliated with the Physicians Coalition for Injectable Safety (PCIS) are hereby granted a license to download, modify and use the materials contained within the *Safety With Injectables™ Workbook* for their individual practices. This license may not be modified or expanded, whether for third party release or to permit either the sale or commercial use of these materials, unless explicit written permission is first obtained from PCIS.

**The updated TOC document calls for a “revised version”.**

**Revised version has not been provided yet. Text herein is old.**

## The Idea in Brief

This is an overview of the Safety With Injectables™ project. The materials supplied within this monograph will allow you to develop your own specific program for injectable safety that will best fit your needs. Having a great process for the use of injectables goes beyond improving quality of outcomes and patient satisfaction, it also provides a framework that thoroughly documents all aspects of using injectables clinically.

### *Getting Started: Safety With Injectables™ Program*

Within this monograph are a variety of templates, documents, and policies/procedures that core injectors can adapt to their individual practices. This is not a “cookbook” approach for injectable safety, but rather the resources developed as the result of expert opinion within a consensus-based framework of the Physician’s Coalition for Injectable Safety. The next step comes down to you to develop your own specific process within your practice: feel free to customize and adapt the material to best suit your needs.

Once you have completed this exercise in injectable safety, you will have defined specific policies and procedures that will help your patients obtain the best and safest outcomes. We believe that the material offered in this monograph will enhance the way you use injectables instead of making it overly complex and burdensome. This material fits well with existing safety and quality programs used by Core-trained injectors. The templates included are adaptable to electronic medical records (EMR).

None of the material contained within this monograph is intended to suggest or establish a particular standard of care. It is provided as a resource to clinicians in order for them to develop their own program of injectable safety, policies and procedures for their use.

### **Leadership**

The physician is ideally suited to lead their staff in developing specific injectable policies and procedures within your practice setting. Clearly designate responsibility for oversight and monitoring. Periodically review staff practices to ensure compliance. Establish procedures and responsibilities for reporting and investigating breaches in infection-control policy and medication errors. Finally, this will be an ongoing process improvement and education activity, especially as new injectables are added to each category.

Patient safety when using injectables helps prevent avoidable catastrophic events resulting from unsafe practices that transmit disease or produce mistakes in medication use.

Many of the concepts elaborated here have their origins in the Toyota Production System and the Lean process improvement for movement in healthcare. These principles have an emphasis on ways to deliver operational excellence, mistake-proof work, and ongoing quality improvement. Both of these approaches are extremely applicable to healthcare. Choose to surround yourself and your employees with a great process for the safe use of cosmetic and therapeutic injectables. It will greatly simplify their use and improve the quality of your outcomes.

#### References:

Graban M. *Lean Hospitals: Improving Quality Patient Safety and Employee Satisfaction*. CRC Press; 2008. [ISBN 978-1-4200-8380-4]

Magee D. *How Toyota Became #1*. Penguin Books; 2007. [ISBN 978-1-59184-179-1]

Spear SJ. Fixing healthcare from the inside, today. *Harvard Business Review*. September 1, 2005.

Stewart TA, Raman AP. Toyota's long drive, an interview with katsuaki watanabe. *Harvard Business Review*. July-August 2007.

## Cosmetic and Therapeutic Injectables: Neurotoxins and Synthetic Fillers

### getting started

**Process Development** Start with a staff meeting to outline the program and develop staff support for the Safety With Injectables Program™

1. Service mapping of process for injectables
  - a. Define what is needed at each point of the process
    - i. Services, staff, documentation, supplies
  - b. Define what procedures, policies, patient education materials, and templates are necessary to ensure a safe and effective process
  - c. Define measures to document and manage potential adverse events (AE's) that can occur following the use of injectables
  - d. Define ways to deliver consistent operational excellence in the use of injectables
2. Have a process to measure quality and patient satisfaction with injectables
3. Have a process to improve the quality of outcomes and fine tune results if necessary
4. Have a process to manage scheduling and recalls for follow up injection treatments
5. Have a process to manage adverse events (AE's) that potentially can occur with the use of injectables.

### Supplies Needed:

Notebook- 3 ring  
Avery tabbed dividers  
High-quality inkjet paper or laser printer 92 brightness  
Inkjet or color laser printer (patient templates are in color)  
Kinko's or similar facility to laminate quick reference guides in plastic

### Disclaimer

The forms, templates, and documents contained within the Safety With Injectables™ Initiative are not intended to represent a standard of care. These documents are offered as a starting point for practitioners to develop their own specific program of policies, procedures, documents, and templates for the safe use of injectables. Each of the components of this initiative must be customized for your particular practice.

**It is recommended that you confirm that there are not any specific regulations regarding restrictions on vial splitting of single use vials or off-label use of injectables in the state where you practice. Additionally, it is important to verify that subordinate injectors are working within the scope of their particular state practice licensing act.**



# policies and procedures



## The Idea in Brief

Each office needs to develop its own specific policies and procedures regarding the 7 topics below. These items serve as a starting point for the development of policies and procedures regarding injectables. It is important that you have your own specific set of policies and procedures regarding injectables, as this will document that you have a specific process for their use according to labeling and off-label use regarding administration in other anatomic areas, vial splitting procedures, and administration beyond the manufacturer's time limit.

Take a few minutes to write policies and procedures for your office/clinic, based on the material in this section that will cover the following topics.

### Office Policies and Procedures

1. Office Policy Regarding Personnel Having Access to Injectables
2. Ordering Procedure for Injectables
3. Policy and Procedure for Reconstitution of Neurotoxin
4. Policy for On-label and Off-label usage Neurotoxin
5. Policy for On-label and Off-label usage Tissue filler
6. Patient Care Pathway for Injectables
7. Emergency Scenarios

#### 1. Office Policy Regarding Personnel Having Access to Injectables

##### Administrative Staff, Medical Office Assistant

- > May order product, receive and unpack shipments, and enter product into inventory

##### Registered Nurses, Physician Assistant (Subordinate Injectors)

- > May order product, receive and unpack shipments and enter product into inventory. Can reconstitute injectables according to established office policy and procedures with sterile technique
- > Can draw up injectables and prepare syringes for injection, according to office policy and procedures with sterile technique
- > Can draw up injectables and prepare syringes for injection, according to office policy and procedures with sterile technique
- > Can administer injectables as a subordinate injector under the direct supervision of physician employer, according to office policy and procedures and the scope of their professional license.

## Physician

- > Can order product, receive and unpack shipments and enter product into inventory
- > Can reconstitute injectables according to established office policy and procedures with sterile technique
- > Can draw up injectables and prepare syringes for injection, according to office policy and procedures with sterile technique
- > Can administer injectables as indicated according to established policies and procedures.

## 2. Ordering Procedure for Injectables:

1. Use of approved vendors and legitimate distribution channels to obtain approved injectables and devices
  - a. Avoidance of illicit product, reimportation, non-approved distribution channels
  - b. Defined vendor for each injectable, contact numbers, and ordering process
2. Documentation of order, fulfillment, and shipping method
3. Documentation of receipt of shipment in good quality

What is needed here: Forms: Order/Receipt

## Receiving, Storage, and Inventory of Injectables

1. Inventory - when received, when used
2. Storage of product according to labeling
3. Safety Engineering
  - a. Segregation of injectables in labeled storage containers/areas to avoid mistakes in usage
  - b. Safety Engineering Chapter, Safety With Injectables™

## 3. Policy and Procedure for Reconstitution of Neurotoxin

### General Principles:

1. Have an established policy for specific injectables that require reconstitution regarding concentration of reconstituted product according to “X” units per cc of injectable, i.e. BOTOX® Cosmetic will be reconstituted with X cc of saline to produce a concentration of XX units/cc for patient use. Generally, a standardized dilution regimen for neurotoxins of “X” units per ml. helps prevent mistakes in dosing.
2. Use of quick reference cards that define volumes of diluent liquid used for reconstitution of specific injectables (Produce in MS Word, laminate in plastic, have available at nursing station where injectables are reconstituted. If different brands of neurotoxins are being used in the same clinical situation, consider printing the quick reference cards on different colors of paper to prevent mistakes).

## Procedure for Reconstitution of Injectables:

1. Wash hands
2. Cleanse work surface with germicidal cleaner
3. Identify product, remove from packaging, verify lot # and expiration date of un-reconstituted product.
4. Do not reconstitute two different brands of neurotoxins simultaneously in order to avoid mistakes
5. Cleanse vial tops with alcohol-impregnated pad
6. Reconstitute injectable according to office policy regarding sterile technique and planned concentration of reconstituted product
7. Dispose of syringes/needles in red medical waste box
8. Label vial:
  - a. Concentration of reconstituted injectable
  - b. Date of reconstitution
  - c. Date of expiration
9. Complete log form to document: lot # reconstitution date, concentration, expiration date
10. Utilize injectable product according to labeling or off-label, discard unused/expired product and vial as medical waste

**What is needed here: Quick Reference Tables For Reconstitution of Specific Brand Neurotoxin, Neurotoxin Reconstitution Form**

## Resources for supplies:

- a. TimeMed Labels ([www.timemed.com](http://www.timemed.com)) TimeMed will make custom stick-on labels. Alternatively, simple mailing labels (Avery) can be used with MS Word to produce specific labels to identify neurotoxins
- b. Rubbermaid™ or Snapware™ plastic containers with lid
- c. Label maker - Brother or Casio brand (office supply store)
- d. Sharpie™ micro tip marker

## 4. Policy for On-label and Off-label Neurotoxin Use

1. On label: Administer neurotoxin in a specific anatomic area, according to labeling. Use neurotoxin vial labeled “for single patient use” “use within “X” time period,” with wastage of unused product according to labeling. If the vial is labeled as a “multi-use vial,” it may be used in this manner, with appropriate infection control precautions.
2. Off-label use: Administer neurotoxin for an indication not in the approved labeling. Use neurotoxin vial labeled “for single patient use” “use within “X” time period” for multiple patients (splitting of vial contents) and beyond labeled time for use.

- a. Alternative Procedure “1” - use vial as a “multi-use” vial, with multiple product withdrawals, each with a new needle/syringe
- b. Alternative Procedure “2” - split vial contents into sub-units, with storage in capped syringes that are appropriately labeled
- c. Alternative Procedure “3” - split vial contents into sub-units, with storage in sterile single-use sterile, non-pyrogenic parenteral medication vials that are appropriately labeled

## Establishing an Expiration Date for Reconstituted Injectables

1. On-label use - establish expiration date according to labeling
2. Off-label use - establish an expiration date “XX” days post reconstitution as part of your office policies and procedures.
3. Ensure that reconstituted product will not be used beyond established expiration date and that unused product reaching expiration date will be discarded as medical waste

## Knowledge base regarding off-label use and storage:

Peer-reviewed scientific articles from medical literature give information regarding off-label storage reconstituted neurotoxins and use beyond labeled “use within “X” hours” and demonstrate that with proper sterile technique that microbial growth within the vial of reconstituted product does not occur.

## Maintenance of potency and Lack of documented microbial growth

### References:

Parsa AA, Lye KD, Parsa FD. Reconstituted botulinum type a neurotoxin: clinical efficacy after long-term freezing before use. *Aesthetic Plast Surg.* 2007 Mar-Apr;31(2):188-91; discussion 192-3.

In contrast to common belief, reconstituted BoNTA may be frozen, thawed, and injected without losing its potency for up to 6 months, with efficacy equivalent to that of freshly prepared BoNTA.

Krishtul A, Lamba A, Bottone EJ, Gordon M. Lack of Microbial Contamination After Prolonged Storage of Partially Used Botulina Toxin A Preparations. *Cosmet Dermatol.* 2002;15(9): 61-64.

25 vials of BTX-A were reconstituted with unpreserved saline and refrigerated at 2 to 8 degrees C for 6 hours to 62 days. After storage, all vials were cultured and tested negative for microbial contamination.

Alam M, Yoo SS, Wrone DA, White LE, Kim JY. Sterility assessment of multiple use botulinum A exotoxin vials: a prospective simulation, *J AM Acad Dermatol.* 2006 Aug;55(2):272-5.

Routine refrigerator storage of medication vials containing reconstituted botulinum toxin does not result in microbial contamination of the contents even after serial re-extraction of solution from these vials, and after handling of such vials by multiple personnel. Storage and subsequent reuse of botulinum toxin appears safe for at least 7 weeks after reconstitution.

Hexsel DM, De Almeida AT, Rutowitsch M et al. Multicenter, double-blind study of the efficacy of injections with botulinum toxin type a reconstituted up to six consecutive weeks before application. *Dermatol Surg.* 2003 May;29(5):523-9.

BTX-A may be applied up to 6 weeks after reconstitution without losing its effectiveness.

Garcia A, Fulton JE Jr. Cosmetic denervation of the muscles of facial expression with botulina toxin, a dose-response study. *Dermatol.* 1996 Jan;22(1):39-43.

Toxin that was reconstituted 30 days produced the same loss of muscle tone as freshly mixed toxin.

Sloop R, Cole BA, Escutin RO. Reconstituted Botulina Toxin Type A Does Not Lose Potency In Humans If It is Refrozen or Refrigerated For Two Weeks Before Use. *Neurology*. 1997;48(1); 249-253.

Reconstituted BTX-A that is subsequently refrigerated or refrozen for two weeks does not lose potency in humans.

Paik NJ, Seo K, Eun HC. Reduced potency after refrigerated storage of botulinum toxin a: human extensor digitorum brevis muscle study movement disorders. *Mov Disord*. 2006 Oct;21(10):1759-63.

Mean compound muscle action potential amplitudes expressed as a percentage of the baseline amplitude were more reduced in sides injected with immediately reconstituted BTA than in sides injected with BTA stored for 1 week or more ( $P < 0.05$ ). No bacterial growth was observed in any stored BTA samples.

## 5. Policy for On-label and Off-label Tissue Filler Use

**On label** use tissue filler according to labeling regarding a specific anatomic area.

**Off-label** use tissue filler for an indication not in the approved labeling

Source: US FDA <http://www.fda.gov/OC/OHRT/IRBS/offlabel.html>

### “Off-Label” Use of Marketed Drugs, Biologics and Medical Devices

Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgment. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product’s use and effects. Use of a marketed product in this manner when the intent is the “practice of medicine” does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by an Institutional Review Board (IRB).

Physicians are not permitted to advertise off-label usage of drugs or devices, as the decision to use them for an indication not in the approved labeling is determined following the establishment of a physician-patient relationship and determination of a therapeutic plan. It is important to document in your medical record the decision to use drugs and devices off-label and to incorporate this into informed consent discussions.

While physicians may discuss off-label usage of drugs and devices as part of CME-related activities, there have been instances of severe penalties and criminal prosecution when off-label usage is promoted during speaker bureau or similar marketing activities. Be certain that issues of compliance with applicable regulations of promotion of drugs and devices are followed.

## 6. Patient Care Pathway for Safe Administration of Injectables

### 1. Obtain medical history including stated interest in undergoing treatment with cosmetic or therapeutic injectable product

- a. List of medications, including non-prescription NSAID, herbs, etc
- b. List of allergies, including latex

2. Perform a focused physical examination regarding the use of injectables
3. Develop treatment plan:
  - a. Review contraindications including patients taking anticoagulants, anti platelet drugs (Plavix®, aspirin, non steroidal anti inflammatory)
  - b. If this is a repeat injection, make assessment of effect and duration of earlier injection treatments, with adjustments/fine tuning as needed
4. Photographic documentation pre/post injection, including animated views if neurotoxin is being injected
5. Informed consent document
6. Documentation of treatment
  - a. Attach or enter label information to medical record, containing lot #, date of reconstitution, concentration, expiration date,
  - b. Document amount of product used and anatomic location(s) of injections
  - c. Disposal of medical waste
7. Follow up call-quality assurance/patient satisfaction/schedule touch up injection if necessary
8. Process for documentation and management of AE's if they occur

## 7. Emergency Situations that Involve injectables

Occasionally, patients will experience physiologic responses to cosmetic injectables such as a vasovagal episode or tachycardia. While these are generally self-limiting, there is the need to manage these events in order that no harm come to your patient. Individuals who experience vasovagal episodes can be injured if they fall and strike the floor. Develop office policies and procedures for situations of vasovagal episodes, tachycardia and similar events.

Other types of events may be more uncommon such as lightheadedness or tachycardia that relates to local anesthetic injections containing epinephrine that may be used for nerve blocks or direct infiltrations prior to filler injections and light-based procedures.

Most surgical offices have crash carts with equipment for monitoring ECG, SaO<sub>2</sub>, blood pressure. Supplemental oxygen/ventilation bag also may be necessary during an event. IV access and medications also may be a consideration if there is an event that requires immediate treatment (anaphylaxis, cardiac arrest, seizure, etc). Otherwise, if a severe event occurs during an injection, it may require calling 911 for paramedic transport to the hospital.

Staff training regarding emergency situations that may occur during cosmetic injection procedures is an additional consideration in developing a comprehensive process of patient safety. Periodic review of emergency procedures and response to situations may be a consideration.

In addition to the aforementioned emergency situations, preparation for adverse events associated with injectables such as accidental intra-arterial injection, skin blanching from arterial occlusion in the lip area, “allergic/anaphylactic” reactions and extremely rare granulomas occurring after cosmetic injectables is a good idea. The Safety With Injectables Workbook contains an Adverse Event form to document the occurrence. Additional considerations would consist of having requisite emergency medications such as parenteral steroids, antihistamines, nitroglycerine paste, low molecular weight heparin, intravenous acetazolamide, hyaluronidase available in the office, depending on the extent of usage of cosmetic injectables. We acknowledge the input of Claudio DeLorenzi, MD from Toronto, Canada on this subject.

The workbook chapter on Adverse Events contains a variety of published references relating to management of injection-related AE’s.



## The Idea in Brief

The importance of having policies and process for infection control when using injectables will prevent disease transmission. Safety engineering will prevent mistakes in medication administration: important references from the Center for Disease Control (CDC) are listed regarding management of needle sticks and exposure to blood/body fluids.

### The Role of Infection Control and Safety Engineering

The Center for Disease Control (CDC) defines these as “Never Events” in which there were breaches in injection safety and infection control. Injection safety includes practices intended to prevent transmission of infectious diseases between one patient and another, between a patient and healthcare provider, and also to prevent harm such as needle stick injuries or exposure to blood-borne pathogens. Safety engineering processes involve steps taken to prevent mistakes in administering injectables to prevent mistakes in administering the wrong injectable, wrong concentration, and incorrect site of injection. The combination of practices to prevent disease transmission and errors with injectables is something that every practice needs.

### Disease transmission can be virtually eliminated if there are established policies and procedures regarding:

- > Hand washing and sanitation of work surface where injectables are prepared
- > Aseptic technique in the handling, reconstitution, and administration of injectables
- > Not leaving needles/syringes inserted into vials - this is a direct route for microbial contamination of vial contents
- > Non reuse of needles, syringes, or gel cooling packs that have had patient contact (dispose as medical waste)
- > Never allowing a needle/syringe that has had patient contact to be reinserted into the medication vial or IV bag/IV line
- > Never recap and store a partially-used syringe of injectable material for future use by the same patient
- > Medications should be discarded upon expiration or any time there are concerns regarding the sterility of the medication
- > Leftover parenteral medications should never be pooled for later administration
- > Use latex or nitrile gloves and universal precautions regarding needle stick injuries and exposure to blood and body fluid



In an ideal world, the contents of an injectable vial would be for a single patient and there would be no multi-use vials. In reality, medication sharing occurs as a common practice. Multi-use vials such as vaccines or local anesthetics are commonly used to treat multiple patients. Other situations relate to a single patient use vial that is split between several patients in an off-label fashion. An example of this is the use of a 100 unit vial of BOTOX Cosmetic® as a multi-use vial. The CDC views these practices with great concern because of the possibility of disease transmission due to breaches in injection safety and infection control. While a vial may be partially used by a single patient and unused product discarded, this becomes a very expensive process.

Provided that all of the precautions listed above are taken, the risk of disease transmission when a vial is split into sub-units is very low. Studies in the medical literature in small series have reported that there is a lack of microbial contamination of vials reconstituted BOTOX® when sterile technique is utilized to withdraw individual aliquots for patient use. Establish within your practice specific policies and procedures regarding the handling, reconstitution, and administration of injectables to prevent disease transmission. Once implemented, these will provide a framework that documents safety and minimizes mistakes.

## Emergency Information Regarding Needlestick Injuries and exposure to blood/body fluid:

The Center for Disease Control (CDC) and the National Institute for Occupational Safety and Health (NIOSH) have the following resources regarding needlestick and exposure to blood/body fluids:

### Internet-based Resources:

- > CDC-NIOSH Blood borne Infectious Disease Home Page:  
<http://www.cdc.gov/niosh/topics/bbp/default.html>
- > Recommendations for Management of Occupational Exposures to Blood  
<http://www.cdc.gov/mmwr/PDF/rr/rr5011.pdf>
- > Emergency Needle stick Information  
<http://www.cdc.gov/niosh/topics/bbp/emrgnedl.html>
- > Post Exposure Prophylaxis Hotline (24Hr.)  
<http://www.nccc.ucsf.edu/Hotlines/PEpline.html>

## The Idea in Brief

Safety engineering can help prevent errors and mistakes in the use of cosmetic and therapeutic injectables. Simple steps are identified that can be implemented by every clinic to help avoid injecting the wrong drug, wrong concentration and wrong site.

### Injectables: Safety Engineering to Reduce Risk of Errors and Mistakes: Neurotoxins and Fillers

This chapter of the workbook is focused on safety engineering to prevent errors in administering the wrong injectable in an incorrect concentration, and in the wrong location.

For many years, there has been only one approved neurotoxin, BOTOX®/BOTOX® Cosmetic (Allergan, Irvine, CA) available in the United States. With the approval of DYSPORT®, there becomes the possibility of mistaking it for BOTOX Cosmetic®. Both DYSPORT® (Ipsen-Medicis, Scottsdale, AZ) and BOTOX®/BOTOX® Cosmetic are unique neurotoxins with slightly different performance characteristics and dosing requirements. Although equivalency ratios have been discussed in publications, it would be safer to use each neurotoxin as a unique drug versus mathematical exercises that could induce errors in dosing and safety.

Both of these drugs are clear, indistinguishable colorless liquids, once reconstituted. If both are being used within the same clinic, mistakes and errors could occur. It is a good idea to develop policies and procedures that would minimize the risk of mistaking these two; neurotoxins and producing adverse events if the wrong one were to be administered in the wrong concentration. Outside of the US, there may be four or more neurotoxins available for clinical use. There is no such entity as a “generic” neurotoxin, which can be used without consideration of pharmacokinetics and biologic response.

### Steps can be taken to avoid mistakes in the use of similar neurotoxins:

- > Store vials of neurotoxins in specific clear plastic boxes with lids (example: Rubbermaid® or Snapware™); label each box accordingly.
- > When starting the process of reconstitution, identify product by brand, remove from packaging, verify lot # and expiration date of un-reconstituted product.
- > Reconstitute each specific neurotoxin according to established policies for potency in terms of “XX” units per ml, with “X” ml of diluent to be used according to the specific neurotoxin. Do not simultaneously reconstitute both in order to avoid mistakes. Use a quick reference sheet that gives specific instructions and volume of diluent used to reconstitute each neurotoxin.

- > Label syringes that contain a specific neurotoxin as to its brand, concentration, and established expiration date- It may be an excellent idea to obtain color-coded custom labels from one of the vendors that produces labels for healthcare (TimeMed Labels, [www.timemed.com](http://www.timemed.com) ). Alternatively, Avery mailing labels can be produced with your computer's word processor that can be color coded and produced on a simple inkjet printer. If there is doubt as to the contents of a syringe of neurotoxin, it must be discarded.
- > Utilize specific worksheets, templates, and informed consents for each brand of neurotoxin. Generic documents only increase the risk of medication errors.
- > Use quick reference sheets that detail dosing of each brand of neurotoxin, according to anatomic area.
- > Verify visually and verbally that you are receiving a specific brand of neurotoxin from a subordinate when injecting a neurotoxin.
- > Do not utilize conversion ratios in which you try to equate "X" units of one neurotoxin brand of equates to "Y" units of the other brand. Each neurotoxin is unique in its pharmacokinetics and effect, dosing regimen and longevity. Each one should be dosed according to training and your clinical experience with each patient, according to their individualized response.
- > Even if you plan to only have one brand of neurotoxin available, consider having established policies and procedures regarding reconstitution of a specific neurotoxin at "XX" units per ml. This implies specific instructions regarding reconstitution of a vial of "XX" units with "X" ml of diluent liquid.

The most straightforward way to avoid mistakes with neurotoxins is to utilize only one of the approved brands versus having two different brands with different dosing requirements and performance characteristics. In reality, many practitioners may elect to have more than one brand of neurotoxin available, just like they do with having an assortment of tissue fillers. The important thing to remember is which one you are using and that you can document a process for its safe use through all persons who have had contact with this class of biological drugs

The other part of this discussion is focused on safety engineering to prevent errors in administering the wrong injectable in an incorrect concentration, and in the wrong location. Tissue fillers within the hyaluronic acid (HA) family look remarkably similar, yet with performance characteristics that are different. Other classification of tissue fillers such as calcium hydroxyl apatite, porcine collagen-based, and polymethylmethacrylate microspheres probably should not be injected in the lips due to reports of lumpiness. While most fillers are used in an off-label fashion at the discretion of the physician to meet patient needs, training is needed to understand where a particular filler works optimally and what anatomic areas should be avoided.

# adverse events with injectables



## The Idea in Brief

Adverse events can occur when injectables are used for cosmetic or therapeutic purposes. Rarely occurring SAE's (serious adverse events) may occur. If adverse events occur, it is worthwhile to document their occurrence. While most AE's can be minor in nature and self-limited, more serious ones may rarely occur that need intervention.

### Adverse Events With Injectables

While there is the possibility of adverse events (AE's) or serious adverse events (SAE'S) occurring every time that a cosmetic or therapeutic injectable is given, the probability of these occurring is small. Often times, normal occurrences associated with injections are wrongly considered to be AE's.

#### Normal occurrences with injections:

- > Bleeding and Bruising
- > Swelling
- > Erythema (Skin Redness)
- > Needle marks
- > Acne-like skin eruptions
- > Skin Lumpiness
- > Asymmetry
- > Pain
- > Accidental Intraarterial injection
- > Vision loss
- > Skin Necrosis
- > Granulomas
- > Allergic Reactions and Hypersensitivity, Anaphylaxis
- > Migration of Tissue Filler or Neurotoxin
- > Chronic Inflammation, Lymphedema, Nodules, Tissue Stiffness (reported with PMMA permanent fillers, Selles, PRS, 2008)

#### AE's and SAE's associated with injectables would consist of the following:

- > Scarring
- > Hyperpigmentation/Hypopigmentation
- > Infection
- > Damage to deeper structures
- > Visible Tissue Filler Material

# adverse events with injectables

>continued

Information supplied by manufacturers in the packaging (DFU, directions for use) contains information regarding the occurrence of AE's and SAE's from clinical studies. Other factors that may be involved are specific anatomic location, type of filler, and experience level of the injector. Published reports in the peer-reviewed medical literature can be used to reference additional AE's and SAE's.

## Unsatisfactory Result

At all times, there is the possibility that cosmetic or therapeutic injections alone may not produce an outcome that meets patient expectations for improvement in wrinkles or soft tissue depressions. There is the possibility of a poor or inadequate response. Additional injections may be necessary. Surgical procedures or other treatments may be recommended in addition to tissue filler treatments. For these reasons, an unsatisfactory result can occur without AE's or SAE's.

The sample informed consents that are part of the Safety With Injectables™ workbook contain explanations of potential AE's, SAE's, and normal occurrences associated with injectables. The possibility of an unsatisfactory outcome is addressed. Patients must acknowledge that they have been informed about risk and consequences and accept responsibility for the clinical decisions that were made along with the financial costs of all future treatments.

## Documentation and Management of AE's and SAE's

Just as you have a process for patient evaluation and planning for the use of injectables, a process to evaluate and treat AE's and SAE's is needed. The workbook contains templates for documenting AE's and SAE's. A quality improvement/patient satisfaction form may also be used here.

If an AE or SAE occurs, try to document it as completely as possible, including photography. The importance of good patient communication and frequency of follow up care must be emphasized. Most of the normal occurrences associated with injections are self-limited and patients need supportive care. AE's and SAE's require more careful treatment and possibly other treatments/procedures. The judicious use of consultants and second opinions to help manage AE's and SAE's is often helpful.

Depending on the AE or SAE, there can be some exacting treatments needed. A reasoned, document approach is optimal versus defaulting to a steroid injection because it is the only tool available. Contact the manufacturer for additional treatment resources and to report the AE/SAE event.

The Toyota Production System's process of asking why may lead to an explanation of AE's and SAE's. Such a process is helpful to gain understanding of the mechanism of AE's and how to prevent them in the future.

# adverse events with injectables

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While the possibility of anaphylaxis and other serious events from injectables is rare, make certain that your office crash cart has necessary supplies (epinephrine, antihistamines, IV fluids, airway support/ventilator bag, and oxygen). Staff training to recognize and manage serious events must be ongoing.

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# adverse events with injectables

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## Acknowledgements:

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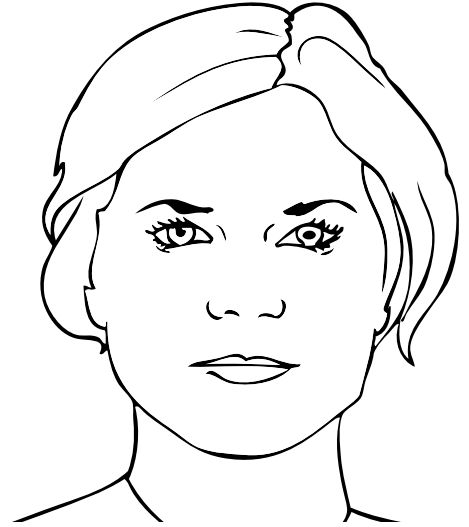
# adverse event template

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## Adverse Event Report Injectables

Date: \_\_\_\_\_

Name: \_\_\_\_\_



Description of Adverse Event: \_\_\_\_\_  
\_\_\_\_\_

Documentation: \_\_\_\_\_

Injectable, lot #, units/amount administered \_\_\_\_\_

Severity: \_\_\_\_\_

Remedy: \_\_\_\_\_

Follow up: \_\_\_\_\_

Form completed by: \_\_\_\_\_

# patient satisfaction with injectables



## The Idea in Brief

Patient satisfaction with the use of cosmetic or therapeutic injectables is paramount to continued success in cosmetic medicine. The quality of the patient's experience determines the suitability of these treatments as something that they are willing to endure on a repeated basis. Besides patient satisfaction, the quality of the outcome is important from a technical perspective. Quality improvement when using injectables should be an ongoing process.

### Quality Improvement/Patient Satisfaction With Injectables

Patient satisfaction with cosmetic and therapeutic injectables is essential to the ongoing success of their use within your practice. Quality improvements should be ongoing. The process should be monitored from the perspective of patient satisfaction, occurrence of adverse events, technical issues, and ways to improve both outcomes and the patient's experience. There should also be ways of solving problems associated with the administration of injectables.

While there is the possibility of adverse events (AE's) or serious adverse events (SAE'S) occurring every time that a cosmetic or therapeutic injectable is given, the probability of these occurring is small. Often times, normal occurrences associated with injections are wrongly considered to be AE's. Even if it's a normal occurrence, it can cause dissatisfaction. Communication skills are necessary to help accurately portray what generally will happen with the use of injectables. Informed consent documents are also necessary to accurately describe both normal and adverse events.

At all times, there is the possibility that cosmetic or therapeutic injections alone may not produce an outcome that meets patient expectations for improvement in wrinkles or soft tissue depressions. There is the possibility of a poor or inadequate response. Additional injections may be necessary. Surgical procedures or other treatments may be recommended in addition to tissue filler treatments.

For these reasons, an unsatisfactory result and dissatisfaction can occur without AE's or SAE's. Just as you have a process for patient evaluation and planning for the use of injectables, there must also be a process to evaluate patient satisfaction and improve quality. A quality improvement/patient satisfaction template is included in the workbook materials.

Other approaches to improve quality and patient satisfaction involve service mapping to

# patient satisfaction with injectables

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understand the steps and resources needed for the use of injectables and patient surveys. Consider using a simple survey regarding comfort during the procedure and the patient's perception of their outcome. From a technical perspective, you may want to document how often you need to perform secondary treatments for "touch ups" or the effectiveness of topical versus nerve blocks for patient comfort. Patient satisfaction and quality are two important parts of the process for using injectables. Improvements and fine tuning is possible if you have a process that incorporates patient feedback and outcome data.

The ability to deliver operational excellence and high level of patient satisfaction when using injectables will differentiate Core trained injectors from others. This in addition to the other components of the *Safety With Injectables™* workbook will help you and your staff achieve better, safer outcomes with injectables.

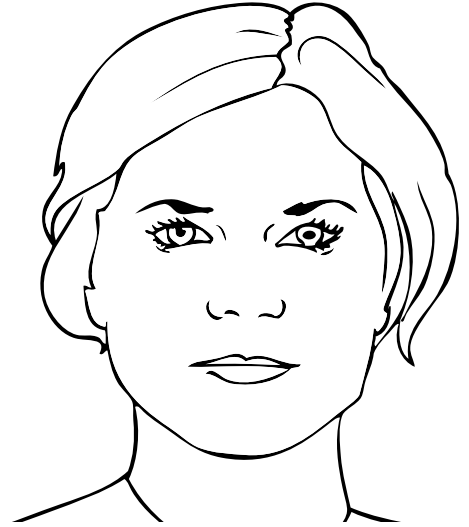
# quality improvement template

>continued

## Quality Assurance-Patient Satisfaction Template

Date: \_\_\_\_\_

Name: \_\_\_\_\_



Injectable used, lot #, units/amount, anatomic area: \_\_\_\_\_

Initial Quality Assessment: Satisfaction/Dissatisfaction: \_\_\_\_\_

Interval Supplemental Injection?: \_\_\_\_\_

Recommendation for future treatment: \_\_\_\_\_

Form completed by: \_\_\_\_\_

# informed consent

- a. Risk Mitigation With Neurotoxins
- b. FDA DYSPORT® Medication Guide
- c. Neurotoxin Consent
- d. HA Filler Consent
- e. Calcium Hydroxylapatite Filler Consent
- f. PMMA Filler Consent
- g. Poly-L Lactic Acid Consent

# informed consent and injectables



## The Idea in Brief

Within this monograph are two sample informed consents for a neurotoxin and hyaluronic acid tissue filler. These can serve as a framework for an informed consent process within your office. The consents can be adapted and customized to specific brands of neurotoxins and fillers.

### Informed Consent and Injectables

There are many different approaches to informed consent for surgical procedures and treatments. Each state has specific requirements for informed consent that must be followed when practicing medicine. In most situations the P-A-R-Q process of discussion of the proposed procedure, listing alternatives, discussion of risk, and answering of questions is the accepted format. While informed consent for a procedure or treatment may be short and fit on a single page of paper, it may not contain specific discussions apropos to the use of injectables. A more detailed informed consent document may be helpful for risk disclosure and delineation of responsibilities.

Each patient processes information differently and informed consent discussions must be accomplished in a way that patients understand both the potential benefits and risks associated with a treatment. Additionally, discussions of financial responsibility are important regarding the potential need to undergo supplementary injections to enhance the results from the initial injection or responsibility for the cost of treating adverse events following use of injectables.

Disclosure of off-label practices regarding indications for injectables outside of labeling is important. It is also a good practice to disclose vial-splitting practices with appropriate safety precautions and the use of reconstituted neurotoxins beyond the manufacturer's established time limit after reconstitution.

# informed consent and injectables

>continued

The process of informed consent when using injectables is straightforward. Have the patient read the consent, initial each page, and sign the last page. A witness must also sign the last page of the consent.

Within this workbook are generic informed consent templates for:

- > Generic neurotoxin
- > Hyaluronic acid tissue filler
- > Porcine collagen gel tissue filler
- > Poly-l lactic acid tissue filler
- > Calcium hydroxyapatite tissue filler
- > Polymethylmethacrylate permanent tissue filler

These documents represent a framework for you to produce your own customized informed consents for specific neurotoxins and hyaluronic acid fillers. Feel free to customize the language, add or delete risk information, etc. Refer to manufacturer's DFU (directions for use) and published literature reports for additional information regarding risk, adverse events, and advisories from the FDA regarding "Black Box Warnings" for neurotoxins. These generic consents can be customized for approved tissue fillers or neurotoxin brand.

**Suggestions for producing customized informed consents:**

Designate a font and font size for the document. The default font is Arial 10 point size. Sans-serif fonts such as Arial or Calibri are easier to read than Times Roman or Courier. Insert a customized header that gives the name of your practice/clinic. Insert your name on the last page of the consent "I hereby authorize Dr. \_\_\_\_\_."

Microsoft Word has a specific find and replace utility (Ctrl-F) that will locate the generic terminology as BONTA and HA in the consents and replace it with brand names such as BOTOX® Cosmetic or DYSPORT® when using neurotoxins or Juvederm Ultra™/UltraPlus™ or Restylane™/Perlane™ when using hyaluronic acid origin tissue fillers. Specific consent documents and treatment templates for each product help reduce medication errors and mistakes.

# informed consent and injectables

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**BE CERTAIN to proofread the document in order to make certain that it is grammatically correct.**

When performing a find and replace operation within MS Word, normal words such as “has” may become garbled when you instruct the program to replace HA with one of the known brand names of hyaluronic acid fillers. It may appear as “Restylanes” or “Juve’derms.”

## **PMMA, Artefill® - Permanent Tissue Filler Additional Advisory Regarding Informed Consent**

The availability of Artefill®, PMMA/collagen permanent tissue filler in the United States is unknown due to the financial collapse of Artes, the distributor for Artefill® in the United States. While this product may be available to practitioners outside of the US, there may not be an approved distributor for it. Practitioners are cautioned to avoid illegal importation of this product into the US from off-shore vendors, as this is considered illegal by the FDA. Additionally, there is not a way to verify that the product is legitimate or has been stored according to manufacturer’s directions. It is also unknown whom will be the responsible for liability of future AE’s from PMMA fillers, given the financial collapse of the US distributor for the product.

An informed consent template for the use of PMMA is included within the workbook, designed for colleagues who are members in the international affiliates of the Physicians Coalition for Injectable Safety. This consent template would not be applicable in countries where PMMA fillers are no longer sold. If Artefill® returns to the US market, the consent template would be applicable

As of May 2009, SUNEVA Medical has purchased the ownership and distribution rights of Artefill®. Their web site is: <http://www.artefill.com/#1>





## The Idea in Brief

The US FDA has determined that Botulinum neurotoxins have the possibility of producing serious adverse events (SAE's) and/or adverse events (AE's). The agency has placed its strongest “boxed warning” on this class of biological and has required a risk evaluation and mitigation strategy (REMS) which includes a patient medication guide to be distributed with the product by the dispensing physician. DYSPORT® (abobotulinumtoxinA) was recently approved with this stipulation; BOTOX®/BOTOX® Cosmetic and Myobloc® will require similar warnings. While it is important to distinguish between the high-unit dosing for functional neuromuscular disorders and the low-unit dosing for cosmetic wrinkle treatments, all of the biologics in this class nevertheless carry these warnings. Communication strategies to address patient questions are an integral part of informed consent for their use.

### Risk Evaluation and Mitigation Strategies for Neurotoxins - Foreward/Introduction: Risk Mitigation (7)

The recent release of DYSPORT®, the second FDA approved neurotoxin designed to treat glabellar wrinkles, it is useful to consider the “boxed warning” as it relates to cosmetic patients. It is very clear that botulinum toxin A used for treatment of cosmetic concerns is amongst the safest in clinical medicine. BOTOX® and BOTOX® Cosmetic are often used synonymously when it comes to public perception, an important false medical myth.

Neurotoxins have been used for more than 30 years to treat a variety of medical conditions, including the treatment of individuals with severe underlying medical conditions that render them “high risk patients” for medical treatments in general. To confuse the use of high dose botulinum toxin for severe, life-impairing conditions with the use of low doses for cosmetic conditions is not appropriate. This lack of differentiation has led to much confusion in the media and amongst physicians in general. It is because of this confusion, we have put together the current material.

In January 2008, a public health advocacy group, Public Citizen reported to the FDA on approximately 16 deaths that were alleged to be related to the use of BOTOX® in the treatment of functional neuromuscular disorders such as cervical dystonia. This involved the alleged injection of high-unit amounts of neurotoxin in compromised patients. According to the Botox® Cosmetic DFU, there was a single patient who died from a fatal case of anaphylaxis in which lidocaine was used as the diluent and consequently the causal agent cannot be reliably determined.

In response to concerns of deaths allegedly associated with the use of neurotoxins to treat functional disorders, the FDA has taken two steps, that of placing a “boxed warning” on all Botulinum neurotoxin containing products and requiring a risk evaluation and mitigation strategy be implemented for this class of biologics.

A “boxed warning” is a type of warning that appears on the package insert for prescription drugs/biologics that may cause serious adverse effects. It is so named for the black border that usually surrounds the text of the warning. This warning means that medical studies indicate that the drug carries a significant risk of serious or even life-threatening AE’s or SAE’s. The U.S. Food and Drug Administration (FDA) can require a pharmaceutical company to place a “boxed warning” on the labeling of a prescription drug and in literature describing its use. It is the strongest warning required by the FDA. There are many drugs that carry these warnings, such as Depo-Provera® for bone loss, Warfarin for bleeding, Retinoids for teratogenic potential and Fluoroquinolone antibiotics for tendon rupture.

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage a known or potential serious risk associated with a drug or biological product. A REMS will be required if FDA finds that a REMS is necessary to ensure that the benefits of the drug or biological product outweigh the risks of the product, and FDA notifies the sponsor. REMS can include a Medication Guide, Patient Package Insert, a communication plan, elements to assure safe use, and an implementation system, and must include a timetable for assessment of the REMS. Some drug and biological products that previously were approved/licensed with risk minimization action plans (Risk MAPs) will now be deemed to have REMS. [http://www.fda.gov/cder/regulatory/FDAAA/FR\\_QA.htm](http://www.fda.gov/cder/regulatory/FDAAA/FR_QA.htm).

Safe use of injectables such as the neurotoxins to treat cosmetic or functional problems does require a discussion with patients regarding the “boxed warning” and the Medication Guide portion of the REMS. Taken at face value, the REMS medication guide for neurotoxins is potentially frightening to patients in terms of all of the SAE’s that might occur following neurotoxin injections. As a document, it lacks balance between mention of the benefits of therapeutic use of neurotoxins and patient satisfaction with outcomes. Most patients do not have the background to process the information contained within this document and to

understand that given millions of neurotoxin injections over many years, there were SAE's and AE's seen in compromised patients who received large-unit injections to treat functional neuromuscular disorders. This is a completely different situation of small-unit injections of neurotoxin for the cosmetic treatment of wrinkles or excessive sweating.

While it is recommended to discuss both the “boxed warning” and the REMS medication guide with patients, each patient processes information differently and informed consent discussions must be accomplished in a way that patients understand both the potential benefits and risks associated with a treatment. Much of this comes down to what would the reasonable person want to know.

## Discussions with patients center around specific dimensions of risk:

1. What are the pertinent undesirable outcomes? (Identification)
2. How permanent is the potential undesirable outcome? (Permanence)
3. When might the unwanted outcome occur? (Timing)
4. What is the probability of the unwanted outcome? (Probability)
5. How significant is the unwanted outcome to the patient? (Subjective badness)

## Patients commonly misinterpret risk:

- > Personal values, biases, and media influences (I read on the web that patients die after neurotoxin injections)
- > Anchoring bias estimate their risks on the basis of familiar risks (“my aunt had eyelid ptosis after neurotoxin injection”)
- > Overestimate a risk factor that has achieved notoriety in the media (death)
- > Compression bias (overestimating small risks and underestimating large risks)
- > Miscalibration of confidence (this will not happen to me)

The question comes then on how outcome data should be presented to patients? It has been shown a long time ago that how these risks are presented will influence decision making. In most situations, qualitative expressions are often more “accessible” to consumers or patients, i.e. “the risk of eyelid ptosis following cosmetic neurotoxin is low” or the risk of eyelid ptosis following cosmetic neurotoxin is less than 3%. Even physicians have trouble sometimes when it comes to talking about relative risk, quantitative risk, attributable risk and the range of confidence associated with statistical evaluation of risk. Other risk dimensions center around how the patient interprets the occurrence as “dreaded” versus something totally “unknown”.

The following pages present data and material is **excerpted** from the product Package Inserts (PI) for BOTOX® Cosmetic (Allergan, Irvine, CA) and DYSPORT® (Medicis, Scottsdale, AZ) when used for cosmetic situations to treat glabellar lines. This represents useful information that injectors can use to discuss risk-related matters with patients contemplating cosmetic neurotoxin injections. For full details, please see the individual product full Package Inserts.

In this specific scenario, the incidence of TEAE's (treatment emergent adverse events) when the biological was used according to labeling and other information from the PI is helpful in addressing questions that patients have regarding safety and efficacy of these two approved neurotoxins for cosmetic improvement of glabellar lines. Other information from the peer-reviewed literature may contain other data that relates risk profile attributable to off-label usage. This information permits a discussion regarding questions that may arise after patients read the REMS Medication Guide that is part of the Dysport package insert.

The data that are contained within the PI include clinical information from clinical trials that were conducted under varying conditions by multiple injectors. The incidence of AE's, SAE's, and TEAE's cannot be compared to rates encountered in the clinical trial of another toxin and may not be predictive of what each injector observes in their practice.

Allergan Botox® Cosmetic (label for use in temporary improvement of glabellar lines) Material excerpted from package insert (PI) (see complete PI document for entire details)

## Indications And Usage

BOTOX® Cosmetic is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients 65 years of age.

## Description

One Unit of BOTOX® Cosmetic corresponds to the calculated median intraperitoneal lethal dose (LD50) in mice. The method utilized for performing the assay is specific to Allergan's product BOTOX® Cosmetic. Due to specific details of this assay such as the vehicle, dilution scheme and laboratory protocols for the various mouse LD50 assays, Units of biological activity of BOTOX® Cosmetic cannot be compared to nor converted into Units of any other botulinum toxin or any toxin assessed with any other specific assay method. In addition, differences in species sensitivities to different botulinum neurotoxin serotypes precludes extrapolation of animal-dose activity relationships to human dose estimates. The specific activity of BOTOX® Cosmetic is approximately 20 units/nanogram of neurotoxin protein complex.

# risk evaluation and mitigation strategies neurotoxins

>continued

## Dosage And Administration - For Intramuscular Injection Only

BOTOX® Cosmetic is to be reconstituted only with 0.9% sterile, non-preserved saline prior to intramuscular injection. Per the dilution table below, draw up the required amount of 0.9% sterile non-preserved sodium chloride solution into a syringe to obtain a reconstituted solution at a concentration of 4.0 Units/0.1 mL and a total treatment dose of 20 Units in 0.5 mL. The duration of activity of BOTOX® Cosmetic for glabellar lines is approximately 3-4 months. The safety and effectiveness of more frequent dosing with BOTOX® Cosmetic has not been clinically evaluated and is not recommended.

## Dilution Technique

Using a 21-gauge needle and an appropriately sized syringe draw up a total of 2.5 mL/100 Unit vial or 1.25 mL/50 Unit vial of 0.9% sterile saline without a preservative. Insert the needle at a 45° angle and slowly inject into the BOTOX® Cosmetic vial. Discard the vial if a vacuum does not pull the diluent into the vial. Gently rotate the vial and record the date and time of reconstitution on the space on the label.

## Dilution Table

Diluent Added to 100 Unit Vial (0.9% Sodium Chloride Only)	Resulting Dose Units per 0.1 mL	Diluent Added to 50 Unit Vial (0.9% Sodium Chloride Only)	Resulting Dose Units per 0.1 mL
2.5 mL	4.0 Units	1.25mL	4.0 Units

## Injection Technique

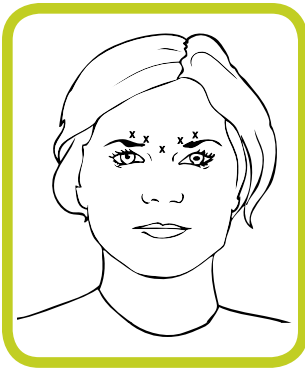
Glabellar facial lines arise from the activity of the corrugator and orbicularis oculi muscles. These muscles move the brow medially, and the procerus and depressor supercilii pull the brow inferiorly. This creates a frown or “furrowed brow.” The location, size, and use of the muscles vary markedly among individuals. Lines induced by facial expression occur perpendicular to the direction of action of contracting facial muscles. An effective dose for facial lines is determined by gross observation of the patient’s ability to activate the superficial muscles injected.

In order to reduce the complication of ptosis the following steps should be taken:

- > Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.

- > Lateral corrugator injections should be placed at least 1 centimeter above the bony supraorbital ridge.
- > Ensure the injected volume/dose is accurate and where feasible kept to a minimum.
- > Do not inject toxin closer than 1 cm above the central eyebrow.

Using a 30-gauge needle, inject a dose of 0.1 mL into each of 5 sites, 2 in each corrugator muscle and 1 in the procerus muscle for a total dose of 20 Units. Typically the initial doses of reconstituted BOTOX® Cosmetic induce chemical denervation of the injected muscles one to two days after injection, increasing in intensity during the first week.



### Precautions

Caution should be used when BOTOX® Cosmetic treatment is used in patients who have an inflammatory skin problem at the injection site, marked facial asymmetry, ptosis, excessive dermatochalasis, deep dermal scarring, thick sebaceous skin or the inability to substantially lessen glabellar lines by physically spreading them apart as these patients were excluded from the Phase 3 safety and efficacy trials.

Needle-related pain and/or anxiety may result in vasovagal responses, (including e.g., syncope, hypotension) which may require appropriate medical therapy.

Injection intervals of BOTOX® Cosmetic should be no more frequent than every three months and should be performed using the lowest effective dose (See: Adverse Reactions, Immunogenicity).

### Geriatric use:

The two clinical studies of BOTOX® Cosmetic did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. However, the responder rates appeared to be higher for patients younger than age 65 than for patients 65 years or older. (See: CLINICAL STUDIES)

### Pregnancy: Pregnancy Category C

Administration of BOTOX® Cosmetic is not recommended during pregnancy. There are no adequate and well-controlled studies of BOTOX® Cosmetic in pregnant women.

### Adverse Reactions

#### General:

BOTOX® and BOTOX® Cosmetic contain the same active ingredient in the same formulation.

Therefore adverse events observed with the use of BOTOX® also have the potential to be associated with the use of BOTOX® Cosmetic.

The most serious adverse events reported after treatment with botulinum toxin include rare spontaneous reports of death, sometimes associated with anaphylaxis, dysphagia, pneumonia, and/or other significant debility. There have also been rare reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease (See: WARNINGS). New onset or recurrent seizures have also been reported, typically in patients who are predisposed to experiencing these events. The exact relationship of these events to the botulinum toxin injection has not been established. Additionally, a report of acute angle closure glaucoma one day after receiving an injection of botulinum toxin for blepharospasm was received, with recovery four months later after laser iridotomy and trabeculectomy. Focal facial paralysis, syncope and exacerbation of myasthenia gravis have also been reported after treatment of blepharospasm.

In general, adverse events occur within the first week following injection of BOTOX® Cosmetic and while generally transient may have a duration of several months or longer. Localized pain, infection, inflammation, tenderness, swelling, erythema and/or bleeding/bruising may be associated with the injection.

## Glabellar Lines:

## Summary Blepharoptosis:

Blepharoptosis incidence	3%
Open label	2%_1% second treatment cycle

In clinical trials of BOTOX® Cosmetic the most frequently reported adverse events following injection of BOTOX® Cosmetic were headache\*, respiratory infection\*, flu syndrome\*, blepharoptosis and nausea.

Less frequently occurring (<3%) adverse reactions included pain in the face, erythema at the injection site\*, paresthesia and muscle weakness. While local weakness of the injected muscle(s) is representative of the expected pharmacological action of botulinum toxin, weakness of adjacent muscles may occur as a result of the spread of toxin. These events are thought to be associated with the injection and occurred within the first week. The events were generally transient but may last several months or longer.

The data described in Table 4 reflect exposure to BOTOX® Cosmetic in 405 subjects

aged 18 to 75 who were evaluated in the randomized, placebo-controlled clinical studies to assess the use of BOTOX® Cosmetic in the improvement of the appearance of glabellar lines (See: CLINICAL STUDIES). Adverse events of any cause were reported for 44% of the BOTOX® Cosmetic treated subjects and 42% of the placebo treated subjects. The incidence of blepharoptosis was higher in the BOTOX® Cosmetic treated arm than in placebo (3% vs. 0). In the open-label, repeat injection study, blepharoptosis was reported for 2% (8/373) of subjects in the first treatment cycle and 1% (4/343) of subjects in the second treatment cycle.

**Immunogenicity:**

Treatment with BOTOX® Cosmetic may result in the formation of neutralizing antibodies that may reduce the effectiveness of subsequent treatments with BOTOX® Cosmetic

**Table 4.** Adverse Events Reported Frequency (>1%) in the BOTOX® Cosmetic Group Compared to the Placebo Group

Adverse Events by Body System	Percent of Patients Reporting Adverse Events	
	BOTOX® Cosmetic (N=405) %	Placebo (N=130) %
Overall	44	42
Body as a Whole Pain in Face	2	1
Skin and Appendages Skin Tightness	1	0
Digestive System Nausea Dyspepsia Tooth Disorder	3 1 1	2 0 0
Special Senses Blepharoptosis	3	0
Musculoskeletal System Muscle Weakness	2	0
Cardiovascular Hypertension	1	0



by inactivating the biological activity of the toxin. The rate of formation of neutralizing antibodies in patients receiving BOTOX® Cosmetic has not been well studied.

The critical factors for neutralizing antibody formation have not been well characterized. The results from some studies suggest that botulinum toxin injections at more frequent intervals or at higher doses may lead to greater incidence of antibody formation. The potential for antibody formation may be minimized by injecting the lowest effective dose given at the longest feasible intervals between injections.

### Postmarketing Experience

Transient ptosis, the most frequently reported complication, has been reported in the literature in approximately 5% of patients. There has been a single report of diplopia, which resolved completely in three weeks.

The following other adverse reactions have been identified since the drug has been marketed: abdominal pain; blurred vision; brachial plexopathy; decreased hearing; diarrhea; ear noise; erythema multiforme; fever; focal facial paralysis; glaucoma; localized numbness; loss of appetite; malaise; myalgia; myasthenia gravis; pruritus; psoriasiform eruption; retinal vein occlusion; sweating; syncope; vertigo with nystagmus, and vomiting.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to botulinum toxin.

### Clinical Studies

#### *Glabellar Lines:*

Two phase 3 randomized, multi-center, double blind, placebo-controlled studies of identical design were conducted to evaluate BOTOX® Cosmetic for use in the temporary improvement of the appearance of moderate to severe glabellar facial lines. The studies enrolled healthy adults (ages 18 to 75) with glabellar lines of at least moderate severity at maximum frown. Patients were excluded if they had ptosis, deep dermal scarring, or an inability to substantially lessen glabellar lines even by physically spreading them apart. Subjects received a single treatment with BOTOX® Cosmetic (N=405, combined studies) or placebo (N=132, combined studies). Injection volume was 0.1 ml/injection site, for a dose/injection site in the active treatment groups of 4 Units. Subjects were injected intramuscularly in five sites, 1 in the procerus muscle and 2 in each corrugator supercilii muscle, for a total dose in the active treatment groups of 20 Units.

The co-primary efficacy endpoints were the investigator's rating of glabellar line severity at maximum frown and the subject's global assessment of change in appearance of glabellar

lines, both at Day 30 post-injection. For the investigator rating, using a 4-point grading scale (0=none, 3=severe) a responder was defined as having a severity grade of 0 or 1. For the subject's global assessment of change, the ratings were from +4 (complete improvement) to -4 (very marked worsening). A responder was defined as having a grade of at least +2 (moderate improvement).

After completion of the randomized studies, subjects were offered participation in an open label, repeat treatment study to assess the safety of repeated treatment sessions.

The combined results of these two efficacy trials are presented here. The mean age was 46 years, with 32 patients (6%) 65 years of age. Most of the subjects (82%) were women, and Caucasian (84%). At baseline, 210 patients (39%) had glabellar line severity scores at rest of moderate or severe. In these studies, the severity of glabellar lines was reduced for up to 120 days in the BOTOX® Cosmetic group compared to the placebo group as measured both by investigator rating of glabellar line severity at maximum frown (Table 1), and by subject's global assessment of change in appearance of glabellar lines (Table 2).

**Table 1.** Investigator's Assessment of Glabellar Line Severity at Maximum Frown- Responder Rates (% and Number of Subjects with Severity of None or Mild)

DAY	BOTOX® Cosmetic	Placebo	DIFFERENCE <sup>a</sup>
7	74% 299/405	6% 8/132	68% (62,74)
30 <sup>b</sup>	80% 325/405	3% 4/132	77% (72,82)
60	70% 283/403	2% 2/130	69% (64,74)
90	48% 192/403	2% 3/128	45% (40,51)
120	25% 102/403	2% 2/128	24% (19,29)

<sup>a</sup> 95% confidence intervals are shown in parenthesis

<sup>b</sup> Day 30: Co-Primary Efficacy Time point, p<0.001

**Table 2.** Subject's Assessment of Change in Appearance of Glabellar Lines - Responder Rates (% and Number of Subjects with at Least Moderate Improvement)

<sup>a</sup> 95% confidence intervals are shown in parenthesis

<sup>b</sup> Day 30: Co-Primary Efficacy Time point,  $p < 0.001$

**Table 3.** Investigator’s and Subject’s Assessment - Responder Rates for Subjects <65 and ≥65 Years of Age at Day 30

ASSESSMENT	AGE GROUP	BOTOX® Cosmetic N=405	PLACEBO N=132	DIFFERENCE <sup>a</sup>
INVESTIGATORS (maximal frown)	< 65	83% 316/382	2% 2/123	81% (77,86)
SUBJECTS	< 65	91% 346/382	7% 8/123	84% (79,90)
INVESTIGATORS (maximal frown)	≥ 65	39% 9/23	22% 2/9	17% (-17,51)
SUBJECTS	≥ 65	70% 16/23	11% 1/9	58% (31,86)

<sup>a</sup> 95% confidence intervals are shown in parenthesis

Exploratory analyses by gender suggested that responder rates in the BOTOX® Cosmetic treated group were higher for women than for men for both the investigator assessment (day 30; 85% of 334 women, 59% of 71 men) and the Subject Assessment (day 30; 93% of women, 72% of men). In the limited number of non-Caucasian patients (n=64 in the BOTOX® Cosmetic treated group) the responder rates were similar to those observed in the Caucasian patients.

**Medicis-DYSPO<sup>®</sup>** (labeled for use in temporary improvement of glabellar lines) (Selected sections from the PI relevant to use in Glabellar Lines)

Material excerpted from package insert (see complete document for entire details) The DYSPO<sup>®</sup> package insert contains the FDA-mandated “black box” warning and the REMS Medication Guide.

### 1.2 Indications and Usage Glabellar Lines

DYSPO<sup>®</sup> (abotulinumtoxinA) is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients <65 years of age.

## **2. Dosage and Administration**

The potency Units of DYSPORT® are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of Botulina toxin products and therefore units of biological activity of DYSPORT® cannot be compared or converted into units of any other Botulina toxin product assessed with any other specific assay method. (Also in 5.1)

### **2.2 Glabellar Lines**

The dose of DYSPORT® for the treatment of glabella lines is a total of 50 units given intramuscularly in five equal aliquots of 10 units each to achieve clinical effect (see figure 1).

#### **2.2.1 Special Populations Adults**

The clinical effect of DYSPORT® may last up to 4 months. Repeated dose clinical studies demonstrated continued efficacy with up to four repeated administrations. It should be administered no more frequently than three months. When used for re-treatment DYSPORT® should be reconstituted and injected using the same techniques as the initial treatment.

#### **2.2.2 Instructions for Preparation and Administration**

DYSPORT® is supplied as a single-use vial.

There are 2 recommended preparation regimens for a 300 unit DYSPORT® vial:

#1: Reconstitute with 2.5ml of 0.9% sterile, preservative-free saline. The concentration of the resulting solution will be 10 units per 0.08ml to be delivered in five equally divided aliquots of 0.08ml each. The concentration of the diluted vial would be 120 units of DYSPORT® per ml.

#2: Reconstitute with 1.5ml of 0.9% sterile, preservative-free saline. The concentration of the resulting solutions will be 10 units per 0.05ml to be delivered in five equally divided aliquots of 0.05ml each. The concentration of the diluted vial would be 200 units of DYSPORT® per ml.

#### **2.2.3 Injection Technique**

Glabellar facial lines arise from the activity of the lateral corrugator and vertical procerus muscles. These can be readily identified by palpating the tensed muscle mass while having the patient frown. The corrugator depresses the skin creating a “furrowed” vertical line surrounded by tensed muscle (i.e., frown lines). The location, size, and use of the muscles vary markedly among individuals. Physicians administering DYSPORT® must understand the relevant neuromuscular and/or orbital anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures. Risk of ptosis can be mitigated by careful examination of the upper lid for separation or weakness of the levator palpebrae muscle

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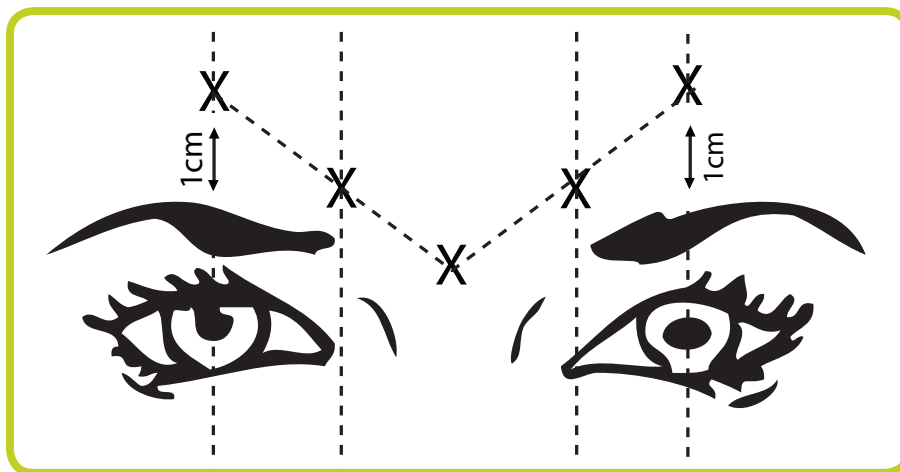
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(true ptosis), identification of lash ptosis, and evaluation of the range of lid excursion while manually depressing the frontalis to assess compensation. In order to reduce the complication of ptosis, the following steps should be taken:

- > Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
- > Medial corrugator injections should be placed at least 1 centimeter above the bony supraorbital ridge.
- > Ensure the injected volume/dose is accurate and where feasible kept to a minimum.
- > Do not inject toxin closer than 1 centimeter above the central eyebrow.

To inject DYSPO<sup>®</sup>, advance the needle through the skin into the underlying muscle while applying finger pressure on the superior medial orbital rim, Inject patients with a total of 50 Units in five equally divided aliquots. Using a 30 gauge needle, inject 10 Units of DYSPO<sup>®</sup> into each of five sites, two in each corrugator muscle, and one in the procerus muscle (see Figure 1).

Figure 1



In the subset of patients with resting severity scores of moderate or severe, the investigator assessment of a resting severity of mild or none at day 30 was also achieved by more BOTOX<sup>®</sup> Cosmetic treated patients (74%, 119/161) than placebo treated patients (20%, 10/49).

Analysis of the limited number of patients 65 years or older suggested lower treatment-associated response compared to patients less than 65 years of age (Table 3).

**Table 4.** Treatment-Emergent Adverse Events (summarized) (TEAE's)

Eyelid ptosis	2%
Headache	9%
Injection site pain	3%
Injection site reaction	3%

**Table 5.** Treatment-emergent Adverse Events with 1% incidence

Adverse Events by Body System	DYSPO <sup>®</sup> n=398 (%)*	Placebo n=496 (%)*
<b>Any Treatment-emergent Adverse Event</b>	191 (48)	163 (33)
<b>Eye Disorders</b>		
Eyelid Edema	8 (2)	0
Eyelid Ptosis	6 (2)	1 (<1)
<b>Gastrointestinal Disorders</b>		
Nausea	6 (2)	5 (1)
<b>General Disorders and Administration Site Conditions</b>		
Injection Site Pain	11 (3)	8 (2)
Injection Site Reaction	12 (3)	2 (<1)
<b>Infections and Infestations</b>		
Nasopharyngitis	38 (10)	21 (4)
Upper Respiratory Tract Infection	12 (3)	9 (2)
Sinusitis	8 (2)	6 (1)
<b>Investigations</b>		
Blood Urine Present	6 (2)	1 (<1)
<b>Nervous System Disorders</b>		
Headache	37 (9)	23 (5)

## Warnings and Precautions

### 5.2 Spread of Toxin Effect

Post marketing safety data from DYSPO<sup>®</sup> and other approved botulinum toxins suggest

that botulinum toxin effects may, in some cases be observed beyond the site of local injection. The symptoms are consistent with the mechanism of action of botulinum toxin and may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties.

## **6. Adverse Reactions**

### **Glabellar Lines**

\*Subjects who received treatment with placebo and DYSPORT® are counted in both treatment columns. In the overall safety database, where some subjects received up to twelve treatments with DYSPORT® adverse events were reported for 57% (142512491) of subjects. The most frequently reported of these adverse events were headache, nasopharyngitis, injection site pain, sinusitis, URI, injection site bruising, and injection site reaction (numbness, discomfort, erythema, tenderness, tingling, itching, stinging, warmth, irritation, tightness, swelling). Adverse events that emerged after repeated injections in 2-3% of the population included bronchitis, influenza, pharyngolaryngeal pain, cough, contact dermatitis, injection site swelling, and injection site discomfort.

The incidence of eyelid ptosis did not increase in the long-term safety studies with multiple re-treatments at intervals  $\geq 3$  months. The majority of eyelid ptosis events were mild to moderate in severity and resolved over several weeks (see injection technique (2.2.3)).

### **6.3 Immunogenicity**

As with all therapeutic proteins, there is a potential for immunogenicity.

#### **Glabellar Lines**

Testing for antibodies to DYSPORT® was performed for 1554 subjects who had up to nine cycles of treatment. Two subjects (0.13%) tested positive for binding antibodies at baseline. Three additional subjects tested positive for binding antibodies after receiving DYSPORT® treatment. None of the subjects tested positive for neutralizing antibodies.

### **8.1 Pregnancy**

*Pregnancy:* Pregnancy Category C

Administration of Dysport® is not recommended during pregnancy. There are no adequate and well-controlled studies of Dysport® in pregnant women.

### **8.6 Ethnic Groups**

Exploratory analysis in trials for glabellar lines in African-American subjects with Fitzpatrick skin types IV, V, or VI and in Hispanic subjects suggested that response at Day 30 were comparable to and no worse than the overall population.

## **14 Clinical Studies**

### **14.2 Glabellar Lines**

Three double-blind, randomized, placebo-controlled, clinical studies evaluated the efficacy of



DYSPO<sup>®</sup> for use in the temporary improvement of the appearance of moderate to severe glabellar lines. These three studies enrolled healthy adults (ages 19-75) with glabellar lines of at least moderate severity at maximum frown. Subjects were excluded if they had marked ptosis, deep dermal scarring, or a substantial inability to lessen glabellar lines, even by physically spreading them apart. The subjects in these studies received either DYSPO<sup>®</sup> or placebo. The total dose was delivered in equally divided aliquots to specified injection sites (see Figure 1).

Investigators and subjects assessed efficacy at maximum frown by using a 4-point scale (none, mild, moderate, severe).

Overall treatment success was defined as post-treatment glabellar line severity of none or mild with at least 2 grade improvement from Baseline for the combined investigator and subject assessments (composite assessment) on Day 30 (see Table 6). Additional endpoints for each of the studies were post-treatment glabellar line severity of none or mild with at least a 1 grade improvement from Baseline for the separate investigator and subject assessments on Day 30. After completion of the randomized studies, subjects were offered participation in a two-year, open-label retreatment study to assess the safety of multiple treatments.

Table 6. Treatment Success at Day 30 (None or Mild with at least 2 Grade Improvement from Baseline at Maximum Frown for the combined Investigator and Subject Assessments (Composite) Treatment with DYSPO<sup>®</sup> reduced the severity of glabellar lines for up to four months.

### **Study GL-1**

Study GL-1 was a single dose, double-blind, multi-center, randomized, placebo-controlled study in which 158 previously untreated subjects received either placebo or 50 Units of DYSPO<sup>®</sup>: administered in five aliquots of 10 Units (see Figure 1). Subjects were followed for 180 days. The mean age was 43 years; most of the subjects were women (85%), and predominantly Caucasian (49%) or Hispanic (47%). At Day 30, 55% of DYSPO<sup>®</sup>-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (see Table 6).

In study GL-1, the reduction of glabellar line severity at maximum frown was greater at Day 30 in the DYSPO<sup>®</sup> group compared to the placebo group as assessed by both investigators and subjects (see Table 7).

### **Study GL-2**

Study GL-2 was a repeat dose, double-blind, multi-center, placebo-controlled, randomized study. The study was initiated with two or three open-label treatment cycles of 50 Units of DYSPO<sup>®</sup> administered in five aliquots of 10 Units DYSPO<sup>®</sup> (see Figure 1). After the open-label treatments, subjects were randomized to receive either placebo or 50 Units of DYSPO<sup>®</sup>. Subjects could have received up to four treatments through the course of the study. Efficacy

**Table 6.** Treatment Success at Day 30 (None or Mild with at least 2 Grade Improvement from Baseline at Maximum Frown for the combined Investigator and Subject Assessments (Composite))

	2 Grade Improvement	
Study	DYSPORT® n/N (%)	Placebo n/N (%)
GL-1	58/105 (55%)	0/53 (0%)
GL-2	37/71 (52%)	0/71 (0%)
GL-3	120/200 (60%)	0/100 (0%)

was assessed in the final randomized treatment cycle. The study enrolled 311 subjects into the first treatment cycle and 142 subjects were randomized into the final treatment cycle. Overall, the mean age was 47 years; most of the subjects were women (86%) and predominantly Caucasian (80%).

At Day 30, 52% of DYSPORT®-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (see Table 6). The proportion of responders in the final treatment cycle was comparable to the proportion of responders in all prior treatment cycles.

After the final repeat treatment with DYSPORT® the reduction of glabellar line severity at maximum frown was greater at Day 30 in the DYSPORT® group compared to the placebo group as assessed by both investigators and subjects (see Table 8).

### Study GL-3

Study GL-3 was a single dose, double-blind, multi-center, randomized, placebo-controlled study in which 300 previously untreated subjects received either placebo or 50 Units of DYSPORT® administered in five aliquots of 10 Units (see Figure 1). Subjects were followed for 150 days. The mean age was 44 years; most of the subjects were women (87%), and predominantly Caucasian (75%) or Hispanic (18%).

At Day 30, 60% of DYSPORT®-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (see Table 6).

In study GL-3, the reduction of glabellar line severity at maximum frown was greater at Day 30 in the DYSPORT® group compared to the placebo group as assessed by both investigators and subjects (see Table 9).

**Table 7.** GL-1: Investigator’s and Subject’s Assessment of Glabellar Line Severity at Maximum Frown Using a 4-point Scale (% and Number of Subjects with Severity of None or Mild)

Day	Investigator’s Assessment		Subject’s Assessment	
	DYSPO <sup>®</sup> N=105	Placebo N=53	DYSPO <sup>®</sup> N=105	Placebo N=53
14	90% 95	17% 9	77% 81	9% 5
30	88% 92	4% 2	74% 78	9% 5
60	64% 67	2% 1	60% 63	6% 3
90	43% 45	6% 3	36% 38	6% 3
120	23% 24	4% 2	19% 20	6% 3
150	9% 9	2% 1	8% 8	4% 2
180	6% 6	0% 0	7% 7	8% 4

### Geriatric Subjects

In GL1, GL2, and GL3, there were 8 subjects aged 65 and older who were randomized to DYSPO<sup>®</sup> 50 Units in 5 equal aliquots of 10 Units (4) or placebo (4). None of the geriatric DYSPO<sup>®</sup> subjects were a treatment success at maximum frown at Day 30.

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BOTOX<sup>®</sup> Cosmetic Package Insert, Allergan, Irvine, CA, USA

DYSPO<sup>®</sup> Package Insert, Medicis, Scottsdale, AZ, USA

**Table 8.** GL-1: Investigator’s and Subject’s Assessment of Glabellar Line Severity at Maximum Frown Using a 4-point Scale (% and Number of Subjects with Severity of None or Mild)

**Table 9.** GL-3: Investigator’s and Subject’s Assessment of Glabellar Line Severity at Maximum Frown Using a 4-point Scale (% and Number of Subjects with Severity of None or Mild)

Day	Investigator’s Assessment		Subject’s Assessment	
	DYSPORT® N=200	Placebo N=100	DYSPORT® N=200	Placebo N=100
14	83% 166	5% 5	83% 165	2% 2
30	86% 171	0% 0	82% 163	2% 2
60	75% 150	1% 1	65% 130	4% 4
90	51% 102	1% 1	46% 91	2% 2
120	29% 58	1% 1	31% 61	3% 3
150	16% 32	1% 1	16% 31	3% 3



**Read the Medication Guide** that comes with DYSPO<sup>®</sup> before you start using it and each time DYSPO<sup>®</sup> is given to you. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment. You should share this information with your family members and caregivers.

### **What is the most important information I should know about DYSPO<sup>®</sup>?**

DYSPO<sup>®</sup> may cause serious side effects that can be life threatening. Call your doctor or get medical help right away if you have any of these problems after treatment with DYSPO<sup>®</sup>:

- > Problems swallowing, speaking, or breathing. These problems can happen hours to weeks after an injection of DYSPO<sup>®</sup> usually because the muscles that you use to breathe and swallow can become weak after the injection. Death can happen as a complication if you have severe problems with swallowing or breathing after treatment with DYSPO<sup>®</sup>.
- > People with certain breathing problems may need to use muscles in their neck to help them breathe. These patients may be at greater risk for serious breathing problems with DYSPO<sup>®</sup>.
- > Swallowing problems may last for several weeks. People who can not swallow well may need a feeding tube to receive food and water. If swallowing problems are severe, food or liquids may go into your lungs. People who already have swallowing or breathing problems before receiving DYSPO<sup>®</sup> have the highest risk of getting these problems.
- > Spread of toxin effects. In some cases, the effect of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. The symptoms of botulism include:
  - > loss of strength and muscle weakness all over the body
  - > double vision
  - > hoarseness or change or loss of voice (dysphonia)
  - > trouble saying words clearly (dysarthria)
  - > loss of bladder control
  - > trouble breathing
  - > trouble swallowing

These symptoms can happen hours to weeks after you receive an injection of DYSPO<sup>®</sup>. These problems could make it unsafe for you to drive a car or do other dangerous activities. See “What should I avoid while receiving DYSPO<sup>®</sup>.”

## What is DYSPO<sup>®</sup>?

DYSPO<sup>®</sup> is a prescription medicine that is injected into muscles and used:

- > to treat the abnormal head position and neck pain that happens with cervical dystonia (CD) in adults
- > to improve the look of moderate to severe frown lines between the eyebrows (glabellar lines) in adults younger than 65 years of age for a short period of time (temporary)

CD is caused by muscle spasms in the neck. These spasms cause abnormal position of the head and often neck pain. After DYSPO<sup>®</sup> is injected into muscles, those muscles are weakened for up to 12 to 16 weeks or longer. This may help lessen your symptoms.

Frown lines (wrinkles) happen because the muscles that control the facial expression are used often (muscle tightening over and over). After DYSPO<sup>®</sup> is injected into the muscle that control facial expression, the medicine stops the tightening of these muscles for up to 4 months.

It is not known whether DYSPO<sup>®</sup> is safe or effective in children under 18 years of age.

It is not known whether DYSPO<sup>®</sup> is safe or effective for the treatment of other types of muscle spasms. It is not known whether DYSPO<sup>™</sup> is safe or effective for the treatment of other wrinkles.

## Who should not take DYSPO<sup>®</sup>?

Do not take DYSPO<sup>®</sup> if you:

- > are allergic to DYSPO<sup>®</sup> or any of the ingredients in DYSPO<sup>®</sup>. See the end of this Medication Guide for a list of ingredients in DYSPO<sup>®</sup>
- > are allergic to cow's milk protein
- > had an allergic reaction to any other botulinum toxin product such as Myobloc<sup>®\*</sup> or BOTOX<sup>®\*</sup>
- > have a skin infection at the planned injection site

## What should I tell my doctor before taking DYSPO<sup>®</sup>?

Tell your doctor about all your medical conditions, including if you have:

- > a disease that affects your muscles and nerves (such as amyotrophic lateral sclerosis [ALS or Lou Gehrig's disease], myasthenia gravis [or Lambert-Eaton syndrome]). See "What is the most important information I should know about DYSPO<sup>®</sup>?"
- > allergies to any botulinum toxin product
- > had any side effect from any botulinum toxin product in the past
- > a breathing problem, such as asthma or emphysema
- > swallowing problems

- > bleeding problems
- > diabetes
- > a slow heart beat or other problem with your heart rate or rhythm
- > plans to have surgery
- > had surgery on your face
- > weakness of your forehead muscles (such as trouble raising your eyebrows)
- > drooping eyelids
- > any other change in the way your face normally looks

**Tell your doctor if you:**

- > are pregnant or plan to become pregnant. It is not known if DYSPO<sup>®</sup> can harm your unborn baby
- > are breast-feeding or planning to breast-feed. It is not known if DYSPO<sup>®</sup> passes into breast milk.

**Tell your doctor about all the medicines you take**, including prescription and nonprescription medicines, vitamins and herbal and other natural products. Using DYSPO<sup>®</sup> with certain other medicines may cause serious side effects. **Do not start any new medicines while taking DYSPO<sup>®</sup> without talking to your doctor first.**

**Especially tell your doctor if you:**

- > have received any other botulinum toxin product in the last four months
- > have received injections of botulinum toxin, such as Myobloc<sup>®</sup> (Botulinum Toxin Type B) or BOTOX<sup>®</sup> (Botulinum Toxin Type A)\* in the past; be sure your doctor knows exactly which product you received
- > have recently received an antibiotic by injection
- > take muscle relaxants
- > take an allergy or cold medicine
- > take a sleep medicine

**Ask your doctor if you are not sure if your medicine is one that is listed above.**

Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine.

**How should I take DYSPO<sup>®</sup>?**

- > DYSPO<sup>®</sup> is an injection that your doctor will give you
- > DYSPO<sup>®</sup> is injected into the affected muscles
- > Your doctor may give you another dose of DYSPO<sup>®</sup> after 12 weeks or longer, if it is needed

- > If you are being treated for CD, your doctor may change your dose of DYSPORT<sup>®</sup> until you and your doctor find the best dose for you
- > The dose of DYSPORT<sup>®</sup> is not the same as the dose of any other botulinum toxin product

### What should I avoid while taking DYSPORT<sup>®</sup>?

DYSPORT<sup>™</sup> may cause loss of strength or general muscle weakness, blurred vision, or drooping eyelids within hours to weeks of taking DYSPORT<sup>®</sup>. If this happens, do not drive a car, operate machinery, or do other dangerous activities. See “What is the most important information I should know about DYSPORT<sup>®</sup>?”

### What are the possible side effects of DYSPORT<sup>®</sup>?

**DYSPORT<sup>®</sup> can cause serious side effects. See “What is the most important information I should know about DYSPORT<sup>®</sup>?”**

Other side effects of DYSPORT<sup>®</sup> include:

- > dry mouth
- > injection site discomfort or pain
- > tiredness
- > headache
- > neck pain
- > muscle pain
- > eye problems: double vision, blurred vision, decreased eyesight, problems with focusing the eyes (accommodation), drooping eyelids, swelling of the eyelids
- > allergic reactions. Symptoms of an allergic reaction to DYSPORT<sup>®</sup> may include: itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint. Tell your doctor or get medical help right away if you get wheezing or asthma symptoms, or if you get dizzy or faint

**Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of DYSPORT<sup>®</sup>. For more information, ask your doctor or pharmacist.**

**Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.**



## General information about DYSPORT<sup>®</sup>:

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

This Medication Guide summarizes the most important information about DYSPORT<sup>®</sup>. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about DYSPORT<sup>®</sup> that is written for healthcare professionals. For more information about DYSPORT<sup>®</sup> call 877-397-7671 or go to [www.dysport.com](http://www.dysport.com) or [www.DysportUSA.com](http://www.DysportUSA.com).

## What are the ingredients in DYSPORT<sup>®</sup>?

Active ingredient: (botulinum toxin Type A)

Inactive ingredients: human albumin, and lactose. DYSPORT<sup>®</sup> may contain cow's milk protein.

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## Instructions

This is an informed-consent document which has been prepared to help inform you concerning cosmetic Botulina-Origin Neurotoxin Type A neurotoxin injections, their risks, and alternative treatments.

It is important that you read this information carefully and completely. Please initial each page, indicating that you have read the page and sign the consent for this procedure as proposed by your physician.

## Instruction

Clostridia botulina bacteria produce a class of chemical compounds known as “toxins.” The Botulina-Origin Neurotoxin Type A “BONTA” is processed and purified to produce a sterile product suitable for specific therapeutic uses. Once the diluted toxin is injected, it produces a temporary paralysis (chemodenervation) of muscle by preventing transmission of nerve impulses to muscle.

BONTA has been used to treat functional disorders that involve muscle spasticity and cosmetic conditions of muscle-induced skin wrinkles of the forehead. It has been used in an “off-label” manner to treat facial wrinkles, excessive sweating, migraine headaches, and colorectal disorders.

Cosmetic BONTA intramuscular injections are customized for every patient, depending on their needs. BONTA cannot stop the process of aging. It can however, temporarily diminish the look of wrinkles caused by muscle groups or treat other conditions.

## US Food and Drug Black Box Warning regarding the administration of neurotoxins:

**Distant Spread of Toxin Effect** Post marketing reports indicate that the effects of all Botulina toxin products may spread from the area of injection to produce symptoms consistent with Botulina toxin effects. This may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. These symptoms have been reported hours to weeks after injections. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity, but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and adults, and in unapproved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.

## Alternative Treatments

Alternative forms of management include not treating the skin wrinkles by any means. Improvement of skin wrinkles may be accomplished by other treatments or alternative types of surgery. Minor skin wrinkling may be improved through chemical skin-peels, lasers, injection of filling material, or other skin treatments. Risks and potential complications are associated with alternative forms of treatment.

## Risks of Bonta (Botulina Type A Toxin) Injections

Every procedure involves a certain amount of risk, and it is important that you understand the risks. Your decision to undergo this procedure is based on the comparison of the risk to potential benefit. Although the majority of patients do not experience the following complications, you should discuss each of them with your physician to make sure you understand the risks, potential complications, and consequences of BONTA injections to improve facial wrinkling.

**Bleeding** - It is possible, though unusual, to have a bleeding episode from a BONTA injection. Bruising may occur. Serious bleeding around the eyeball during deeper BONTA injections for crossed eyes (strabismus) has occurred. Should you develop post-injection bleeding, it may require emergency treatment or surgery. Do not take any aspirin or anti-inflammatory medications for seven days before BONTA injections, as this may contribute to a greater risk of bleeding.

**Damage to deep structures** - Deeper structures such as nerves, blood vessels, and the eyeball may be damaged during the course of BONTA injection. Injury to deeper structures may be temporary or permanent.

**Pain** - Discomfort associated with BONTA injections is usually short in duration. It is possible to have a fainting episode (vasovagal) from discomfort or anxiety about the injections. Headaches have been reported post BONTA injection.

**Migration of BONTA** - BONTA may migrate from its original injection site to other areas and produce temporary paralysis of other muscle groups or other unintended effects (see FDA “Black Box” warning page 1).

**Skin disorders** - Skin rash and swelling may rarely occur following BONTA injection.

## Eye-related problems:

- > Corneal exposure problems - Some patients experience difficulties closing their eyelids after BONTA injections and problems may occur in the cornea due to dryness. Should this rare complication occur, additional treatments, protective eye drops, contact lenses, or surgery may be necessary.
- > Dry eye problems - Individuals who normally have dry eyes may be advised to use special caution in considering BONTA injections around the eyelid region.
- > Drooping Eyelid (Ptosis) - Muscles that raise the eyelid may be affected by BONTA, should this material migrate downward from other injection areas.
- > Double Vision - Double vision may be produced if the BONTA migrates into the region of muscles that control movements of the eyeball.
- > Eyelid Ectropion - Abnormal looseness of the lower eyelid can occur following BONTA injection.
- > Other Eye Disorders - Functional and irritative disorders of eye structures may rarely occur following BONTA injections.
- > Blindness - Blindness is extremely rare after BONTA injections. However, it can be caused by internal bleeding around the eyeball or needle stick injury.

**Asymmetry** -The human face and eyelid region is normally asymmetrical with respect to structural anatomy and function. There can be a variation from one side to the other in terms of the response to BONTA injection.

**Unknown risks** - The long term effect of BONTA on tissue is unknown. There is the possibility that additional risk factors may be discovered.

**Unsatisfactory result** - There is the possibility of a poor or inadequate response from BONTA injection. Additional BONTA injections may be necessary.

**Allergic reactions** - As with all biologic products, allergic and systemic anaphylactic reactions may occur. Allergic reactions may require additional treatment.

**Antibodies to BONTA** - Presence of antibodies to BONTA may reduce the effectiveness of this material in subsequent injections. The health significance of antibodies to BONTA is unknown.

**Long-term effects** - Subsequent alterations in face and eyelid appearance may occur as the result of aging, weight loss or gain, sun exposure, or other circumstances not related to BONTA injections. BONTA injection does not arrest the aging process or produce permanent tightening of the eyelid region. Future surgery or other treatments may be necessary.

## Risks of BONTA Injections, continued

**Infection** - Infection is extremely rare after BONTA injection. BONTA is contraindicated if there is an infection at the injection site.

**Pregnancy and nursing mothers** - Animal reproduction studies have not been performed to determine if BONTA could produce fetal harm. It is not known if BONTA can be excreted in human milk.

**Drug Interactions** - The effect of BONTA may be potentiated by aminoglycoside antibiotics or other drugs known to interfere with neuromuscular transmission.

**Off-label usage of BONTA** - BONTA, depending on its manufacturer is labeled for specific use. The use of BONTA for other conditions and disorders would be considered “off-label” usage by your physician. FDA defines off label use as, “Use for indication, dosage form, dose regimen, population or other use parameter not mentioned in the approved labeling.” The FDA recognizes that off label use of drugs by prescribers is often appropriate and may receive endorsement from published literature. BONTA may be used according to a physician’s practice beyond the manufacturer’s time limit following reconstitution. Contents of a BONTA vial may be split into sub-units and given to multiple patients, using appropriate sterile technique and precautions.

## Health Insurance

Most health insurance companies exclude coverage for cosmetic surgical procedures and treatments or any complications that might occur from the same. Please carefully review your health insurance subscriber information pamphlet.

## Additional Treatment Necessary

There are many variable conditions in addition to risk and potential complications that may influence the long term result of BONTA injections. Even though risks and complications occur infrequently, the risks cited are the ones that are particularly associated with BONTA injections. Other complications and risks can occur but are even more uncommon. Should complications occur, other treatments may be necessary. The practice of medicine and surgery is not an exact science. Although good results are expected, there is no guarantee or warranty expressed or implied, on the results that may be obtained.

## Financial Responsibilities

The cost of BONTA injection may involve several charges. This includes the professional fee for the injections, follow up visits to monitor the effectiveness of the treatment, and the

cost of the BONTA product. It is unlikely that BONTA injections to treat cosmetic problems would be covered by your health insurance. Additional costs of medical treatment would be your responsibility should complications develop from BONTA injections. You may require additional treatments with BONTA to enhance the effect of the initial treatment.

## Disclaimer

Informed-consent documents are used to communicate information about the proposed surgical treatment of a disease or condition along with disclosure of risks and alternative forms of treatment(s). The informed-consent process attempts to define principles of risk disclosure that should generally meet the needs of most patients in most circumstances.

However, informed-consent documents should not be considered all-inclusive in defining other methods of care and risks encountered. Your physician may provide you with additional or different information which is based on all of the facts pertaining to your particular case and the state of medical knowledge.

Informed-consent documents are not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all of the facts involved in an individual case and are subject to change as scientific knowledge and technology advance and as practice patterns evolve.

**It is important that you read the above information carefully and have all of your questions answered before signing the consent on the next page.**

## CONSENT FOR SURGERY/PROCEDURE or TREATMENT

1. I hereby authorize Dr. \_\_\_\_\_ and such assistants as have been selected to perform the following procedure or treatment:

I have received the following information sheet:  
INFORMED-CONSENT for BONTA Injection  
Medication Guide Document for Neurotoxins

2. I recognize that during the course of the operation and medical treatment or anesthesia, unforeseen conditions may necessitate different procedures than those above. I therefore authorize the above physician and assistants or designees to perform such other procedures that are in the exercise of his or her professional judgment necessary and desirable. The authority granted under this paragraph shall include all conditions that require treatment and are not known to my physician at the time the procedure is begun.
3. I consent to the administration of local anesthesia (regional nerve blocks , direct infiltration, or topical) to diminish discomfort of injection.
4. I acknowledge that no guarantee has been given by anyone as to the results that may be obtained.
5. I consent to the photographing or televising of the operation(s) or procedure(s) to be performed, including appropriate portions of my body, for medical, scientific or educational purposes, provided my identity is not revealed by the pictures.
6. For purposes of advancing medical education, I consent to the admittance of observers to the treatment room.
7. IT HAS BEEN EXPLAINED TO ME IN A WAY THAT I UNDERSTAND:  
a. THE ABOVE TREATMENT OR PROCEDURE TO BE UNDERTAKEN  
b. THERE MAY BE ALTERNATIVE PROCEDURES OR METHODS OF TREATMENT  
c. THERE ARE RISKS TO THE PROCEDURE OR TREATMENT PROPOSED

I CONSENT TO THE TREATMENT OR PROCEDURE AND THE ABOVE LISTED ITEMS (1-7). I AM SATISFIED WITH THE EXPLANATION.

\_\_\_\_\_  
Patient or Person Authorized to Sign for Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness

# hyaluronic acid tissue fillers (ha)

## Instructions

This is an informed-consent document which has been prepared to help inform you concerning HA Tissue Filler injection therapy, its risks, and alternative treatments.

It is important that you read this information carefully and completely. Please initial each page, indicating that you have read the page and sign the consent for this procedure as proposed.

## Introduction

Hyaluronic acid is a naturally occurring substance that is found within all mammals. It is a material that is contained in various soft tissues. Hyaluronic acid is synthetically produced from a process of bacterial fermentation, chemically stabilized, and purified for use as an injectable soft tissue filler.

HA tissue filler has been approved to treat areas of facial wrinkling and soft tissue depressions.

HA tissue filler injections are customized for every patient, depending on their particular needs. These can be performed in areas involving the face and eyelid region, forehead, and lips. HA tissue filler cannot stop the process of aging. It can however, temporarily diminish the appearance of wrinkles and soft tissue depressions. HA tissue filler injections may be performed as a singular procedure, in combination with other treatments such as neurotoxins, or as an adjunct to a surgical procedure. HA tissue injections require regional nerve blocks or topical anesthetic to diminish discomfort. Soft tissue fillers produce temporary swelling, redness, and needle marks, which resolve after a few days time.

Continuing treatments are necessary in order to maintain the effect of tissue fillers over time. HA tissue filler once injected will be slowly absorbed by the body. The length of effect for tissue filler injections is variable.

## Alternative Treatments

Alternative forms of management include not treating the skin wrinkles or soft tissue depressions by any means. Improvement of skin wrinkles and soft tissue depressions may be accomplished by other treatments: laser treatments, chemical skin-peels, other skin procedures, or dermabrasion, alternative types of tissue fillers, or surgery such as a blepharoplasty, face or brow lift when indicated. Risks and potential complications are associated with alternative forms of medical or surgical treatment.

## Risks Of Ha Tissue Filler Injections

Every procedure to inject soft tissue filler materials involves a certain amount of risk, and it is important that you understand the risks involved. An individual's choice to undergo this procedure is based on the comparison of the risk to potential benefit. Although the majority



# hyaluronic acid tissue fillers (ha)

>continued

of patients do not experience the following, you should discuss each of them with your physician to make sure you understand the risks, potential complications, limitations, and consequences of HA tissue filler injections. Additional information may be obtained from the package-insert sheets supplied by the manufacturer.

Problems associated with the use of tissue fillers can relate to normal occurrences following tissue filler injections, or potential complications following tissue filler injections, including HA tissue filler. Additional advisory information should be reviewed by patients considering tissue filler treatments that involve HA tissue filler.

## Normal occurrences during tissue filler injections, including HA TISSUE FILLER

Patients undergoing injections of HA tissue filler may normally experience the following events:

**Bleeding and Bruising** - It is possible, though unusual, to have a bleeding episode from an injection or local anesthesia used during the procedure. Bruising in soft tissues may occur. Should you develop post-injection bleeding, it may require emergency treatment or surgery. Aspirin, anti-inflammatory medications, platelet inhibitors, anticoagulants, Vitamin E, Ginkgo biloba and other “herbs/homeopathic remedies” may contribute to a greater risk of a bleeding problem. Do not take any of these for seven days before injections. Bleeding and bruising can produce permanent tissue color changes.

**Swelling** - Swelling (edema) is a normal occurrence following the injections. It decreases after a few days. If swelling is slow to resolve, medical treatment may be necessary.

**Erythema (Skin Redness)** - Erythema in the skin occurs after injections. It can be present for a few days after the procedure.

**Needle marks** - Visible needle marks from the injections occur normally and resolve in a few days.

**Acne-like skin eruptions** - Acneiform skin eruptions can occur following the injection of tissue fillers. This generally resolves within a few days.

**Skin Lumpiness** - Lumpiness can occur following the injection of HA tissue filler. This tends to smooth out over time. In some situations, it may be possible to feel the injected tissue filler material for long periods of time.

**Asymmetry** - The human face and eyelid region is normally asymmetrical in its appearance and anatomy. It may not be possible to achieve or maintain exact symmetry with tissue filler injections. There can be a variation from one side to the other in terms of the response to HA tissue filler injection. This may require additional injections to improve your outcome.

# hyaluronic acid tissue fillers (ha)

>continued

**Pain** - Discomfort associated with tissue filler injections is normal and usually of a short duration. It is possible to have a fainting episode (vasovagal) from discomfort or anxiety about the injections.

## **Complications (adverse events)**

Potential complications attributable to the injection of soft tissue fillers, including HA tissue filler:

**Infection** - Although infection following injection of tissue fillers is unusual, bacterial, fungal, and viral infections can occur. Herpes simplex virus infections around the mouth, can occur following a tissue filler treatment. This applies to both individuals with a past history of Herpes simplex virus infections and individuals with no known history of Herpes simplex virus infections in the mouth area. Specific medications must be prescribed and taken both prior to and following the treatment procedure in order to suppress an infection from this virus. Should any type of skin infection occur, additional treatment including antibiotics may be necessary.

**Damage to deeper structures** - Deeper structures such as nerves, blood vessels, and the soft tissues may be damaged during the course of injection. Injury to deeper structures may be temporary or permanent.

**Visible Tissue Filler Material** - It may be possible to see any type of tissue filler material that was injected in areas where the skin is thin.

**Skin Necrosis** - It is very unusual to experience death of skin and deeper soft tissues after HA tissue filler injections. Skin necrosis can produce unacceptable scarring. Should this rare complication occur, additional treatments, or surgery may be necessary.

**Granulomas** - Painful masses in the skin and deeper tissues after a HA tissue filler injection are extremely rare. Should these occur, additional treatments including antibiotics or surgery may be necessary. Granulomas may produce scarring within the skin and deeper structures.

**Allergic Reactions and Hypersensitivity** - As with all biologic products, allergic reactions may occur. Allergic reactions may require additional treatment. It is unknown if HA tissue filler is associated with serious systemic anaphylactic allergic reactions.

**Antibodies to HA TISSUE FILLER** - Presence of antibodies to HA tissue fillers may in theory reduce the effectiveness of this material or produce a reaction in subsequent injections. The health significance of antibodies to hyaluronic acid tissue fillers is unknown.

# hyaluronic acid tissue fillers (ha)

>continued

**Accidental Intraarterial injection** - It is extremely rare that during the course of injection, that tissue filler could be accidentally injected into arterial structures and produce a blockage of blood flow. This may produce skin necrosis in facial structures or damage blood flow to the eye, resulting in loss of vision. The risk and consequences of accidental intravascular injection is unknown and not predictable.

**Under/Over Correction** - The injection of soft tissue fillers to correct wrinkles and soft tissue contour deficiencies may not produce the desired outcome. The amount of correction may be inadequate or excessive. It may not be possible to control the process of injection of tissue fillers due to factors attributable to each patient's situation. If under correction occurs, you may be advised to consider additional injections of tissue filler materials. Over correction may require removal of tissue filler material.

## **Additional Advisories**

Advisories for patients considering non-permanent tissue filler injections:

**Off-label usage of HA** - HA, depending on its manufacturer is labeled for specific use. The use of HA for other conditions and disorders would be considered "off-label" usage by your physician. FDA defines off label use as, "Use for indication, dosage form, dose regimen, population or other use parameter not mentioned in the approved labeling." The FDA recognizes that off label use of drugs by prescribers is often appropriate and may receive endorsement from published literature. HA may be used according to a physician's practice to treat other conditions.

**Unsatisfactory Result** - HA tissue filler injections alone may not produce an outcome that meets your expectations for improvement in wrinkles or soft tissue depressions. There is the possibility of a poor or inadequate response. Additional injections may be necessary. Surgical procedures or other treatments may be recommended in addition to tissue filler treatments.

**Unknown Risks** - There is the possibility that additional risks and complications attributable to the use of tissue fillers may be discovered.

**Migration of Tissue Filler** - Product may migrate from its original injection site and produce visible fullness in adjacent tissue or other unintended effects.

**Drug and Local Anesthetic Reactions** - There is the possibility that a systemic reaction could occur from either the topical or local anesthetic or epinephrine used for sensory nerve block anesthesia when tissue filler injections are performed. This would include the possibility of light-headedness, rapid heart beat (tachycardia), and fainting. Medical treatment of these conditions may be necessary.

# hyaluronic acid tissue fillers (ha)

>continued

**Combination of Procedures** - In some situations, neurotoxin injections or other types of tissue filler materials may be used in addition to HA tissue filler in order to specifically treat areas of the face or to enhance the outcome from tissue filler therapy. The effect of other forms of external skin treatments (laser and other light therapies, microdermabrasion, dermabrasion, or chemical peels) on skin that has been treated with tissue fillers is unknown. The effect of HA tissue filler injections into tissue that has been formerly treated with other types of temporary or permanent tissue fillers is unknown.

**Pregnancy and Nursing Mothers** - Animal reproduction studies have not been performed to determine if HA tissue filler could produce fetal harm. It is not known if HA tissue filler or its breakdown products can be excreted in human milk. It is not recommended that pregnant women or nursing mothers receive tissue filler treatments.

**Drug Interactions** - It is not known if HA tissue filler reacts with other drugs within the body.

**Long-Term Effects** - HA tissue filler injections should not be considered as a permanent treatment for the correction of wrinkles and soft tissue depressions. Over time, the HA tissue filler material is slowly absorbed by the body and wrinkles or soft tissue depressions will reappear. Continuing HA tissue filler treatment (injections) are necessary in order to maintain the effect. Subsequent alterations in face and eyelid appearance may occur as the result of aging, weight loss or gain, sun exposure, or other circumstances not related to tissue filler injections. Future surgery or other treatments may be necessary. Tissue filler injections do not arrest the aging process or produce permanent tightening of the skin or improvement in wrinkles.

## **Health Insurance**

Most health insurance companies exclude coverage for cosmetic surgical procedures and treatments or any complications that might occur from the same. Health insurance companies may not pay for tissue filler injections used to treat medical conditions. Please carefully review your health insurance subscriber information pamphlet.

## **Additional Treatment Necessary**

There are many variable conditions in addition to risk and potential complications that may influence the long-term result of HA tissue filler injections. Even though risks and complications occur infrequently, the risks cited are the ones that are particularly associated with HA tissue filler injections. Other complications and risks can occur but are even more uncommon. Should complications occur, additional surgery or other treatments may be necessary. You are advised to seek medical care should complications or adverse events

# hyaluronic acid tissue fillers (ha)

>continued

occur after tissue filler treatments. Although good results are expected, there is no guarantee or warranty expressed or implied, on the results that may be obtained with the use of HA tissue filler injections. The practice of medicine and surgery is not an exact science.

## Financial Responsibilities

This treatment provides a defined amount of HA tissue filler for the treatment of wrinkles and other conditions. If additional interim injections of HA tissue filler are needed in order to maintain or improve results, you will be responsible for these costs in addition to the cost of this treatment session. It is unlikely that tissue filler injections to treat cosmetic problems would be covered by your health insurance. Additional costs of medical treatment would be your responsibility should complications develop from HA tissue filler injections. You would also be responsible for additional forms of treatments or surgery recommended to improve the appearance of facial wrinkles and soft tissue depressions. In signing the consent for this surgery/procedure, you acknowledge that you have been informed about its risk and consequences and accept responsibility for the clinical decisions that were made along with the financial costs of all future treatments.

## Disclaimer

Informed-consent documents are used to communicate information about the proposed treatment of a disease or condition along with disclosure of risks and alternative forms of treatment(s). The informed-consent process attempts to define principles of risk disclosure that should generally meet the needs of most patients in most circumstances.

However, informed-consent documents should not be considered all-inclusive in defining other methods of care and risks encountered. Your physician may provide you with additional or different information which is based on all of the facts pertaining to your particular case and the state of medical knowledge.

Informed-consent documents are not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all of the facts involved in an individual case and are subject to change as scientific knowledge and technology advance and as practice patterns evolve.

**It is important that you read the above information carefully and have all of your questions answered before signing the consent on the next page.**

# hyaluronic acid tissue fillers (ha)

>continued

## CONSENT FOR SURGERY/PROCEDURE or TREATMENT

1. I hereby authorize Dr. \_\_\_\_\_ and such assistants as have been selected to perform the following procedure or treatment:

\_\_\_\_\_ HA TISSUE FILLER INJECTIONS: \_\_\_\_\_

I have received the following information sheet:  
INFORMED-CONSENT for HA TISSUE FILLER Injection

2. I acknowledge that no guarantee has been given by anyone as to the results that may be obtained.
3. I consent to the administration of local anesthesia (regional nerve blocks , direct infiltration, or topical) to diminish discomfort of injection.
4. I consent to the photographing or televising of the operation(s) or procedure(s) to be performed, including appropriate portions of my body, for medical, scientific or educational purposes, provided my identity is not revealed by the pictures.
5. For purposes of advancing medical education, I consent to the admittance of observers to the treatment room.
6. IT HAS BEEN EXPLAINED TO ME IN A WAY THAT I UNDERSTAND:
- a. THE ABOVE TREATMENT OR PROCEDURE TO BE UNDERTAKEN
  - b. THERE MAY BE ALTERNATIVE PROCEDURES OR METHODS OF TREATMENT
  - c. THERE ARE RISKS TO THE PROCEDURE OR TREATMENT PROPOSED
  - d. THAT I ACCEPT RESPONSIBILITY FOR THE CLINICAL DECISIONS MADE ALONG WITH THE FINANCIAL COSTS OF ALL FUTURE TREATMENTS TO REVISE, OPTIMIZE OR IMPROVE OUTCOMES.

I CONSENT TO THE TREATMENT OR PROCEDURE AND THE ABOVE LISTED ITEMS (1-6). I AM SATISFIED WITH THE EXPLANATION THAT I HAVE RECEIVED BEFORE DECIDING TO UNDERGO THE TREATMENT OR PROCEDURE. I ACCEPT RESPONSIBILITY FOR THE RISKS, CONSEQUENCES, AND BENEFITS OF THIS DECISION.

\_\_\_\_\_  
Patient or Person Authorized to Sign for Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness

## Instructions

This is an informed-consent document which has been prepared to help inform you concerning CaHA Tissue Filler injection therapy, its risks, and alternative treatments. It is important that you read this information carefully and completely. Please initial each page, indicating that you have read the page and sign the consent for this procedure as proposed.

## Introduction

Calcium hydroxyapatite is a calcium-containing substance found in bone and teeth. It can be formulated into a tissue filler material by forming it into micro beads and mixing it with a gel material for use as a tissue filler.

CaHA tissue filler has been approved to treat moderate to severe folds and wrinkles.

CaHA tissue filler injections are customized for every patient, depending on their particular needs. These can be performed in areas involving the face and eyelid region and forehead. CaHA tissue filler cannot stop the process of aging. It can however, temporarily diminish the appearance of wrinkles and soft tissue depressions. CaHA tissue filler injections may be performed as a singular procedure, in combination with other treatments such as neurotoxins, or as an adjunct to a surgical procedure. CaHA tissue injections require regional nerve blocks or topical anesthetic to diminish discomfort. Soft tissue fillers produce temporary swelling, redness, and needle marks, which resolve after a few days time.

Continuing treatments are necessary in order to maintain the effect of tissue fillers over time. CaHA tissue filler once injected will be slowly absorbed by the body. The length of effect for tissue filler injections is variable.

## Alternative Treatments

Alternative forms of management include not treating the skin wrinkles or soft tissue depressions by any means. Improvement of skin wrinkles and soft tissue depressions may be accomplished by other treatments: laser treatments, chemical skin-peels, other skin procedures, or dermabrasion, alternative types of tissue fillers, or surgery such as a blepharoplasty, face or brow lift when indicated. Risks and potential complications are associated with alternative forms of medical or surgical treatment.

## Risks Of CaHA Tissue Filler Injections

Every procedure to inject soft tissue filler materials involves a certain amount of risk, and it is important that you understand the risks involved. An individual's choice to undergo this procedure is based on the comparison of the risk to potential benefit. Although the majority of patients do not experience the following, you should discuss each of them with your physician to make sure you understand the risks, potential complications, limitations, and consequences

of CaHA tissue filler injections. Additional information may be obtained from the package-insert sheets supplied by the manufacturer.

Problems associated with the use of tissue fillers can relate to normal occurrences following tissue filler injections, or potential complications following tissue filler injections, including CaHA tissue filler. Additional advisory information should be reviewed by patients considering tissue filler treatments that involve CaHA tissue filler.

Normal occurrences during tissue filler injections, including CaHA TISSUE FILLER  
Patients undergoing injections of CaHA tissue filler may normally experience the following events:

**Bleeding and Bruising** - It is possible, though unusual, to have a bleeding episode from an injection or local anesthesia used during the procedure. Bruising in soft tissues may occur. Should you develop post-injection bleeding, it may require emergency treatment or surgery. Aspirin, anti-inflammatory medications, platelet inhibitors, anticoagulants, Vitamin E, Ginko biloba and other “herbs/homeopathic remedies” may contribute to a greater risk of a bleeding problem. Do not take any of these for seven days before injections. Bleeding and bruising can produce permanent tissue color changes.

**Swelling** - Swelling (edema) is a normal occurrence following the injections. It decreases after a few days. If swelling is slow to resolve, medical treatment may be necessary.

**Erythema (Skin Redness)** - Erythema in the skin occurs after injections. It can be present for a few days after the procedure.

**Needle marks** - Visible needle marks from the injections occur normally and resolve in a few days.

**Acne-like skin eruptions** - Acneiform skin eruptions can occur following the injection of tissue fillers. This generally resolves within a few days.

**Skin Lumpiness** - Lumpiness can occur following the injection of CaHA tissue filler. This tends to smooth out over time. In some situations, it may be possible to feel the injected tissue filler material for long periods of time.

**Asymmetry** - The human face and eyelid region is normally asymmetrical in its appearance and anatomy. It may not be possible to achieve or maintain exact symmetry with tissue filler injections. There can be a variation from one side to the other in terms of the response to CaHA tissue filler injection. This may require additional injections to improve your outcome.

**Pain** - Discomfort associated with tissue filler injections is normal and usually of a short duration. It is possible to have a fainting episode (vasovagal) from discomfort or anxiety about the injections.



## Complications (adverse events)

Potential complications attributable to the injection of soft tissue fillers, including CaHA tissue filler:

**Infection** - Although infection following injection of tissue fillers is unusual, bacterial, fungal, and viral infections can occur. Herpes simplex virus infections around the mouth, can occur following a tissue filler treatment. This applies to both individuals with a past history of Herpes simplex virus infections and individuals with no known history of Herpes simplex virus infections in the mouth area. Specific medications must be prescribed and taken both prior to and following the treatment procedure in order to suppress an infection from this virus. Should any type of skin infection occur, additional treatment including antibiotics may be necessary.

**Damage to deeper structures** - Deeper structures such as nerves, blood vessels, and the soft tissues may be damaged during the course of injection. Injury to deeper structures may be temporary or permanent.

**Visible Tissue Filler Material** - It may be possible to see any type of tissue filler material that was injected in areas where the skin is thin. CaHA tissue filler material is visible on x-ray and CT scans.

**Skin Necrosis** - It is very unusual to experience death of skin and deeper soft tissues after CaHA tissue filler injections. Skin necrosis can produce unacceptable scarring. Should this rare complication occur, additional treatments, or surgery may be necessary. Injections of CaHA into the glabellar folds is contraindicated because of tissue necrosis risk. Fistula and extrusion may occur following CaHA injections.

**Pruritis (Itching)** - Itching has been reported following injection of CaHA tissue filler material.

**Granulomas** - Masses (lumps) in the skin and deeper tissues after a CaHA tissue filler injection are extremely rare. Should these occur, additional treatments including antibiotics or surgery may be necessary. Granulomas may produce scarring within the skin and deeper structures.

**Allergic Reactions and Hypersensitivity** - It is unknown if CaHA tissue filler is associated with serious systemic anaphylactic allergic reactions.

**Accidental Intraarterial injection** - It is extremely rare that during the course of injection, that tissue filler could be accidentally injected into arterial structures and produce a blockage of blood flow. This may produce skin necrosis in facial structures or damage blood flow to the eye, resulting in loss of vision. The risk and consequences of accidental intravascular injection is unknown and not predictable.

**Under/Over Correction** - The injection of soft tissue fillers to correct wrinkles and soft tissue contour deficiencies may not produce the desired outcome. The amount of correction may be inadequate or excessive. It may not be possible to control the process of injection of tissue fillers due to factors attributable to each patient's situation. If under correction occurs, you may be advised to consider additional injections of tissue filler materials. Over correction may require removal of tissue filler material.

## **Additional Advisories**

Advisories for patients considering semi-permanent tissue filler injections: Off-label usage of CaHA- CaHA, depending on its manufacturer is labeled for specific use. The use of CaHA for other conditions and disorders would be considered "off-label" usage by your physician. FDA defines off label use as, "Use for indication, dosage form, dose regimen, population or other use parameter not mentioned in the approved labeling." The FDA recognizes that off label use of drugs by prescribers is often appropriate and may receive endorsement from published literature. CaHA may be used according to a physician's practice to treat other conditions.

**Unsatisfactory Result** - CaHA tissue filler injections alone may not produce an outcome that meets your expectations for improvement in wrinkles or soft tissue depressions. There is the possibility of a poor or inadequate response. Additional injections may be necessary. Surgical procedures or other treatments may be recommended in addition to tissue filler treatments.

**Unknown Risks** - There is the possibility that additional risks and complications attributable to the use of tissue fillers may be discovered.

**Migration of Tissue Filler** - Product may migrate from its original injection site and produce visible fullness in adjacent tissue or other unintended effects.

**Drug and Local Anesthetic Reactions** - There is the possibility that a systemic reaction could occur from either the topical or local anesthetic or epinephrine used for sensory nerve block anesthesia when tissue filler injections are performed. This would include the possibility of light-headedness, rapid heart beat (tachycardia), and fainting. Medical treatment of these conditions may be necessary.

**Combination of Procedures** - In some situations, neurotoxin injections or other types of tissue filler materials may be used in addition to CaHA tissue filler in order to specifically treat areas of the face or to enhance the outcome from tissue filler therapy. The effect of other forms of external skin treatments (laser and other light therapies, microdermabrasion, dermabrasion, or chemical peels) on skin that has been treated with tissue fillers is unknown. The effect

of CaHA tissue filler injections into tissue that has been formerly treated with other types of temporary or permanent tissue fillers is unknown. It is not recommended that CaHA be injected into areas treated with liquid silicone or particle fillers

**Pregnancy and Nursing Mothers** - Animal reproduction studies have not been performed to determine if CaHA tissue filler could produce fetal harm. It is not known if CaHA tissue filler or its breakdown products can be excreted in human milk. It is not recommended that pregnant women or nursing mothers receive tissue filler treatments.

**Drug Interactions** - It is not known if CaHA tissue filler reacts with other drugs within the body.

**Long-Term Effects**- CaHA tissue filler injections should not be considered as a permanent treatment for the correction of wrinkles and soft tissue depressions. Over time, the CaHA tissue filler material is slowly absorbed by the body and wrinkles or soft tissue depressions will reappear. Continuing CaHA tissue filler treatment (injections) are necessary in order to maintain the effect. Subsequent alterations in face and eyelid appearance may occur as the result of aging, weight loss or gain, sun exposure, or other circumstances not related to tissue filler injections. Future surgery or other treatments may be necessary. Tissue filler injections do not arrest the aging process or produce permanent tightening of the skin or improvement in wrinkles.

## Health Insurance

Most health insurance companies exclude coverage for cosmetic surgical procedures and treatments or any complications that might occur from the same. Health insurance companies may not pay for tissue filler injections used to treat medical conditions. Please carefully review your health insurance subscriber information pamphlet.

## Additional Treatment Necessary

There are many variable conditions in addition to risk and potential complications that may influence the long-term result of CaHA tissue filler injections. Even though risks and complications occur infrequently, the risks cited are the ones that are particularly associated with CaHA tissue filler injections. Other complications and risks can occur but are even more uncommon. Should complications occur, additional surgery or other treatments may be necessary. You are advised to seek medical care should complications or adverse events occur after tissue filler treatments. Although good results are expected, there is no guarantee or warranty expressed or implied, on the results that may be obtained with the use of CaHA tissue filler injections. The practice of medicine and surgery is not an exact science.

## Financial Responsibilities

This treatment provides a defined amount of CaHA tissue filler for the treatment of wrinkles and other conditions. If additional interim injections of CaHA tissue filler are needed in order to maintain or improve results, you will be responsible for these costs in addition to the cost of this treatment session. It is unlikely that tissue filler injections to treat cosmetic problems would be covered by your health insurance. Additional costs of medical treatment would be your responsibility should complications develop from CaHA tissue filler injections. You would also be responsible for additional forms of treatments or surgery recommended to improve the appearance of facial wrinkles and soft tissue depressions.

**In signing the consent for this surgery/procedure, you acknowledge that you have been informed about its risk and consequences and accept responsibility for the clinical decisions that were made along with the financial costs of all future treatments.**

## Disclaimer

Informed-consent documents are used to communicate information about the proposed treatment of a disease or condition along with disclosure of risks and alternative forms of treatment(s). The informed-consent process attempts to define principles of risk disclosure that should generally meet the needs of most patients in most circumstances.

However, informed-consent documents should not be considered all-inclusive in defining other methods of care and risks encountered. Your physician may provide you with additional or different information which is based on all of the facts pertaining to your particular case and the state of medical knowledge.

Informed-consent documents are not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all of the facts involved in an individual case and are subject to change as scientific knowledge and technology advance and as practice patterns evolve.

**It is important that you read the above information carefully and have all of your questions answered before signing the consent on the next page.**

## CONSENT FOR SURGERY/PROCEDURE or TREATMENT

1. I hereby authorize Dr. \_\_\_\_\_ and such assistants as have been selected to perform the following procedure or treatment:

\_\_\_\_\_ CaHA TISSUE FILLER INJECTIONS: \_\_\_\_\_

I have received the following information sheet:  
INFORMED-CONSENT for CaHA TISSUE FILLER Injection

2. I acknowledge that no guarantee has been given by anyone as to the results that may be obtained.
3. I consent to the administration of local anesthesia (regional nerve blocks , direct infiltration, or topical) to diminish discomfort of injection.
4. I consent to the photographing or televising of the operation(s) or procedure(s) to be performed, including appropriate portions of my body, for medical, scientific or educational purposes, provided my identity is not revealed by the pictures.
5. For purposes of advancing medical education, I consent to the admittance of observers to the treatment room.
6. IT HAS BEEN EXPLAINED TO ME IN A WAY THAT I UNDERSTAND:
- a. THE ABOVE TREATMENT OR PROCEDURE TO BE UNDERTAKEN
  - b. THERE MAY BE ALTERNATIVE PROCEDURES OR METHODS OF TREATMENT
  - c. THERE ARE RISKS TO THE PROCEDURE OR TREATMENT PROPOSED
  - d. THAT I ACCEPT RESPONSIBILITY FOR THE CLINICAL DECISIONS MADE ALONG WITH THE FINANCIAL COSTS OF ALL FUTURE TREATMENTS TO REVISE, OPTIMIZE OR IMPROVE OUTCOMES.

I CONSENT TO THE TREATMENT OR PROCEDURE AND THE ABOVE LISTED ITEMS (1-6). I AM SATISFIED WITH THE EXPLANATION THAT I HAVE RECEIVED BEFORE DECIDING TO UNDERGO THE TREATMENT OR PROCEDURE. I ACCEPT RESPONSIBILITY FOR THE RISKS, CONSEQUENCES, AND BENEFITS OF THIS DECISION.

\_\_\_\_\_  
Patient or Person Authorized to Sign for Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness

## Instructions

This is an informed-consent document which has been prepared to help inform you concerning PMMA Tissue Filler injection therapy, its risks, and alternative treatments. It is important that you read this information carefully and completely. Please initial each page, indicating that you have read the page and sign the consent for this procedure as proposed.

## Introduction

Polymethylmethacrylate is a synthetic polymer. It is a material that is formed into microscopic-sized beads and mixed with bovine-origin collagen. It is injected as permanent soft tissue filler. Once injected, the collagen component is absorbed, leaving the PMMA beads. PMMA tissue filler has been approved to treat the areas of nasolabial folds. A skin test injection with collagen tissue filler is necessary prior to the PMMA tissue filler treatment to determine that patients are not allergic to the bovine collagen contained with the PMMA tissue filler material.

PMMA tissue filler injections are customized for every patient, depending on their particular needs. PMMA tissue filler cannot stop the process of aging. It can however, diminish the appearance of wrinkles and soft tissue depressions. PMMA Tissue Filler injections may be performed as a singular procedure, in combination with other treatments such as neurotoxins, or as an adjunct to a surgical procedure. PMMA tissue injections require regional nerve blocks or topical anesthetic to diminish discomfort. Soft tissue fillers produce temporary swelling, redness, and needle marks, which resolve after a few days time.

## Alternative Treatments

Alternative forms of management include not treating the skin wrinkles or soft tissue depressions by any means. Improvement of skin wrinkles and soft tissue depressions may be accomplished by other treatments: laser treatments, chemical skin-peels, other skin procedures, or dermabrasion, alternative types of tissue fillers, or surgery such as a blepharoplasty, face or brow lift when indicated. Risks and potential complications are associated with alternative forms of medical or surgical treatment.

## Risks Of Pmma Tissue Filler Injections

Every procedure to inject soft tissue filler materials involves a certain amount of risk, and it is important that you understand the risks involved. An individual's choice to undergo this procedure is based on the comparison of the risk to potential benefit. Although the majority of patients do not experience the following, you should discuss each of them with your physician to make sure you understand the risks, potential complications, limitations, and consequences of permanent PMMA tissue filler injections. Additional information may be obtained from the package-insert sheets supplied by the manufacturer.

Problems associated with the use of tissue fillers can relate to normal occurrences following tissue filler injections, or potential complications following tissue filler injections, including PMMA tissue filler. Additional advisory information should be reviewed by patients considering tissue filler treatments that involve PMMA tissue filler.

## Normal occurrences during tissue filler injections, including PMMA TISSUE FILLER

Patients undergoing injections of PMMA tissue filler may normally experience the following events:

**Bleeding and Bruising** - It is possible, though unusual, to have a bleeding episode from an injection or local anesthesia used during the procedure. Bruising in soft tissues may occur. Should you develop post-injection bleeding, it may require emergency treatment or surgery. Aspirin, anti-inflammatory medications, platelet inhibitors, anticoagulants, Vitamin E, Ginkgo biloba and other “herbs/homeopathic remedies” may contribute to a greater risk of a bleeding problem. Do not take any of these for seven days before injections. Bleeding and bruising can produce permanent tissue color changes.

**Swelling** - Swelling (edema) is a normal occurrence following the injections. It decreases after a few days. If swelling is slow to resolve, medical treatment may be necessary.

**Erythema (Skin Redness)** - Erythema in the skin occurs after injections. It can be present for a few days after the procedure.

**Needle marks** - Visible needle marks from the injections occur normally and resolve in a few days.

**Acne-like skin eruptions** - Acneiform skin eruptions can occur following the injection of tissue fillers. This generally resolves within a few days.

**Skin Lumpiness** - Lumpiness can occur following the injection of PMMA tissue filler. In some situations, it may be possible to feel the injected tissue filler material for long periods of time.

**Asymmetry** - The human face and eyelid region is normally asymmetrical in its appearance and anatomy. It may not be possible to achieve or maintain exact symmetry with tissue filler injections. There can be a variation from one side to the other in terms of the response to PMMA tissue filler injection. This may require additional injections to improve your outcome.

**Pain** - Discomfort associated with tissue filler injections is normal and usually of a short duration. It is possible to have a fainting episode (vasovagal) from discomfort or anxiety about the injections.

## Complications (adverse events)

Potential complications attributable to the injection of permanent soft tissue fillers, including PMMA tissue filler:

**Infection** - Although infection following injection of tissue fillers is unusual, bacterial, fungal, and viral infections can occur. **Herpes simplex virus** infections around the mouth, can occur following a tissue filler treatment. This applies to both individuals with a past history of Herpes simplex virus infections and individuals with no known history of Herpes simplex virus infections in the mouth area. Specific medications must be prescribed and taken both prior to and following the treatment procedure in order to suppress an infection from this virus. Should any type of skin infection occur, additional treatment including antibiotics may be necessary.

**Damage to deeper structures** - Deeper structures such as nerves, blood vessels, and the soft tissues may be damaged during the course of injection. Injury to deeper structures may be temporary or permanent.

**Visible Tissue Filler Material** - It may be possible to see any type of tissue filler material that was injected in areas where the skin is thin.

**Skin Necrosis** - It is very unusual to experience death of skin and deeper soft tissues after PMMA tissue filler injections. Skin necrosis can produce unacceptable scarring. Should this rare complication occur, additional treatments, or surgery may be necessary.

**Granulomas** - Painful masses in the skin and deeper tissues after a PMMA tissue filler injection are rare. Should these occur, additional treatments including antibiotics, injections, or surgery may be necessary. Granulomas may produce scarring within the skin and deeper structures.

**Lip complications** - Lip complications, such as stiffness, lymphedema, and nodules have been reported in patients who underwent lip injections with PMMA permanent tissue fillers.

**Allergic Reactions and Hypersensitivity** - As with all biologic products, allergic reactions may occur. PMMA permanent tissue fillers contain bovine collagen. Individuals with a known allergy to bovine collagens should not undergo PMMA permanent tissue filler injections. Allergic reactions may require additional treatment. It is unknown if PMMA tissue filler is associated with serious systemic anaphylactic allergic reactions.



**Antibodies to PMMA TISSUE FILLER** - Presence of antibodies to collagen component of PMMA tissue fillers may in theory reduce the effectiveness of this material or produce a reaction in subsequent injections. The health significance of antibodies is unknown.

**Accidental Intraarterial injection** - It is extremely rare that during the course of injection, that tissue filler could be accidentally injected into arterial structures and produce a blockage of blood flow. This may produce skin necrosis in facial structures or damage blood flow to the eye, resulting in loss of vision. The risk and consequences of accidental intravascular injection is unknown and not predictable.

**Under/Over Correction** - The injection of soft tissue fillers to correct wrinkles and soft tissue contour deficiencies may not produce the desired outcome. The amount of correction may be inadequate or excessive. It may not be possible to control the process of injection of tissue fillers due to factors attributable to each patient's situation. If under correction occurs, you may be advised to consider additional injections of tissue filler materials. Over correction may require removal of tissue filler material.

## Additional Advisories

Advisories for patients considering non-permanent tissue filler injections: Off-label usage of PMMA- PMMA is labeled for specific use approved to treat areas of deep facial wrinkles such as nasolabial folds. The use of PMMA for other conditions and disorders would be considered "off-label" usage by your physician. FDA defines off label use as, "Use for indication, dosage form, dose regimen, population or other use parameter not mentioned in the approved labeling." The FDA recognizes that off label use of drugs by prescribers is often appropriate and may receive endorsement from published literature. PMMA may be used according to a physician's practice to treat other conditions.

**Unsatisfactory Result** - PMMA tissue filler injections alone may not produce an outcome that meets your expectations for improvement in wrinkles or soft tissue depressions. There is the possibility of a poor or inadequate response. Additional injections may be necessary. Surgical procedures or other treatments may be recommended in addition to tissue filler treatments. Complications and adverse events associated with permanent fillers may be of greater severity and permanence than temporary fillers.

**Unknown Risks** - There is the possibility that additional risks and complications attributable to the use of tissue fillers may be discovered. There is the risk of adverse and serious adverse events occurring years following the injection of all permanent fillers, including PMMA.

**Migration of Tissue Filler** - Product may migrate from its original injection site and produce visible fullness in adjacent tissue or other unintended effects.

**Drug and Local Anesthetic Reactions** - There is the possibility that a systemic reaction could occur from either the topical or local anesthetic or epinephrine used for sensory nerve block anesthesia when tissue filler injections are performed. This would include the possibility of light-headedness, rapid heart beat (tachycardia), and fainting. Medical treatment of these conditions may be necessary.

**Pregnancy and Nursing Mothers** - Animal reproduction studies have not been performed to determine if PMMA tissue filler could produce fetal harm. It is not known if PMMA tissue filler or its breakdown products can be excreted in human milk. It is not recommended that pregnant women or nursing mothers receive tissue filler treatments.

**Combination of Procedures** - In some situations, neurotoxin injections or other types of tissue filler materials may be used in addition to PMMA tissue filler in order to specifically treat areas of the face or to enhance the outcome from tissue filler therapy. The effect of other forms of external skin treatments (laser and other light therapies, microdermabrasion, dermabrasion, or chemical peels) on skin that has been treated with tissue fillers is unknown. The effect of PMMA tissue filler injections into tissue that has been formerly treated with other types of temporary or permanent tissue fillers is unknown.

**Drug Interactions** - It is not known if PMMA tissue filler reacts with other drugs within the body. Long-Term Effects- PMMA tissue filler injections should not be considered as a permanent treatment for the correction of wrinkles and soft tissue depressions. Subsequent alterations in face and eyelid appearance may occur as the result of aging, weight loss or gain, sun exposure, or other circumstances not related to tissue filler injections. Future surgery or other treatments may be necessary. Tissue filler injections do not arrest the aging process or produce permanent tightening of the skin or improvement in wrinkles. .

## Health Insurance

Most health insurance companies exclude coverage for cosmetic surgical procedures and treatments or any complications that might occur from the same. Health insurance companies may not pay for tissue filler injections used to treat medical conditions. Please carefully review your health insurance subscriber information pamphlet.

## Additional Treatment Necessary

There are many variable conditions in addition to risk and potential complications that may influence the long-term result of PMMA tissue filler injections. Even though risks and complications occur infrequently, the risks cited are the ones that are particularly associated with PMMA tissue filler injections. Other complications and risks can occur but are even

more uncommon. Should complications occur, additional surgery or other treatments may be necessary. You are advised to seek medical care should complications or adverse events occur after tissue filler treatments. Although good results are expected, there is no guarantee or warranty expressed or implied, on the results that may be obtained with the use of PMMA tissue filler injections. The practice of medicine and surgery is not an exact science.

## Financial Responsibilities

This treatment provides a defined amount of PMMA tissue filler for the treatment of wrinkles and other conditions. If additional interim injections of PMMA tissue filler are needed in order to maintain or improve results, you will be responsible for these costs in addition to the cost of this treatment session. It is unlikely that tissue filler injections to treat cosmetic problems would be covered by your health insurance. Additional costs of medical treatment would be your responsibility should complications develop from PMMA tissue filler injections. You would also be responsible for additional forms of treatments or surgery recommended to improve the appearance of facial wrinkles and soft tissue depressions.

**In signing the consent for this surgery/procedure, you acknowledge that you have been informed about its risk and consequences and accept responsibility for the clinical decisions that were made along with the financial costs of all future treatments.**

## Disclaimer

Informed-consent documents are used to communicate information about the proposed treatment of a disease or condition along with disclosure of risks and alternative forms of treatment(s). The informed-consent process attempts to define principles of risk disclosure that should generally meet the needs of most patients in most circumstances.

However, informed-consent documents should not be considered all-inclusive in defining other methods of care and risks encountered. Your physician may provide you with additional or different information which is based on all of the facts pertaining to your particular case and the state of medical knowledge.

Informed-consent documents are not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all of the facts involved in an individual case and are subject to change as scientific knowledge and technology advance and as practice patterns evolve.

**It is important that you read the above information carefully and have all of your questions answered before signing the consent on the next page.**

## CONSENT FOR SURGERY/PROCEDURE or TREATMENT

1. I hereby authorize Dr. \_\_\_\_\_ and such assistants as have been selected to perform the following procedure or treatment:

\_\_\_\_\_ PMMA TISSUE FILLER INJECTIONS: \_\_\_\_\_

I have received the following information sheet:  
INFORMED-CONSENT for PMMA TISSUE FILLER Injection

2. I acknowledge that no guarantee has been given by anyone as to the results that may be obtained.
3. I consent to the administration of local anesthesia (regional nerve blocks , direct infiltration, or topical) to diminish discomfort of injection.
4. I consent to the photographing or televising of the operation(s) or procedure(s) to be performed, including appropriate portions of my body, for medical, scientific or educational purposes, provided my identity is not revealed by the pictures.
5. For purposes of advancing medical education, I consent to the admittance of observers to the treatment room.
6. IT HAS BEEN EXPLAINED TO ME IN A WAY THAT I UNDERSTAND:
  - a. THE ABOVE TREATMENT OR PROCEDURE TO BE UNDERTAKEN
  - b. THERE MAY BE ALTERNATIVE PROCEDURES OR METHODS OF TREATMENT
  - c. THERE ARE RISKS TO THE PROCEDURE OR TREATMENT PROPOSED
  - d. THAT I ACCEPT RESPONSIBILITY FOR THE CLINICAL DECISIONS MADE ALONG WITH THE FINANCIAL COSTS OF ALL FUTURE TREATMENTS TO REVISE, OPTIMIZE OR IMPROVE OUTCOMES.

I CONSENT TO THE TREATMENT OR PROCEDURE AND THE ABOVE LISTED ITEMS (1-6). I AM SATISFIED WITH THE EXPLANATION THAT I HAVE RECEIVED BEFORE DECIDING TO UNDERGO THE TREATMENT OR PROCEDURE. I ACCEPT RESPONSIBILITY FOR THE RISKS, CONSEQUENCES, AND BENEFITS OF THIS DECISION.

\_\_\_\_\_  
Patient or Person Authorized to Sign for Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness



## Instructions

This is an informed-consent document which has been prepared to help inform you concerning PLL Tissue Filler injection therapy, its risks, and alternative treatments.

It is important that you read this information carefully and completely. Please initial each page, indicating that you have read the page and sign the consent for this procedure as proposed.

## Introduction

Poly-l lactic acid (PLL) is a synthetic tissue filler material that is a polymer of lactic acid molecules. Lactic acid polymers have been used to produce absorbable suture and orthopedic bone screws/plates. A suspension of PLL is used as a tissue filler

PLL tissue filler is intended for aesthetic correction of shallow to deep nasolabial fold contour deficiencies and other facial wrinkles in which a deep dermal grid pattern (cross hatch) injection technique is used.

PLL tissue filler injections are customized for every patient, depending on their particular needs. These can be performed in other areas of the face, such as lower eyelid region, forehead, and jawline (all are off-label). PLL tissue filler cannot stop the process of aging. It can however, temporarily diminish the appearance of wrinkles and soft tissue depressions. PLL Tissue Filler injections may be performed as a singular procedure, in combination with other treatments such as neurotoxins, or as an adjunct to a surgical procedure. PLL tissue injections require regional nerve blocks or topical anesthetic to diminish discomfort. Soft tissue fillers produce temporary swelling, redness, and needle marks, which resolve after a few days time.

Continuing treatments are necessary in order to maintain the effect of tissue fillers over time. PLL tissue filler once injected will be slowly absorbed by the body. The length of effect for tissue filler injections is variable. PLL tissue filler treatments require several injection sessions to produce an effect.

## Alternative Treatments

Alternative forms of management include not treating the skin wrinkles or soft tissue depressions by any means. Improvement of skin wrinkles and soft tissue depressions may be accomplished by other treatments: laser treatments, chemical skin-peels, other skin procedures, or dermabrasion, alternative types of tissue fillers, or surgery such as a blepharoplasty, face or brow lift when indicated. Risks and potential complications are associated with alternative forms of medical or surgical treatment.

## Risks Of PLL Tissue Filler Injections

Every procedure to inject soft tissue filler materials involves a certain amount of risk, and it is important that you understand the risks involved. An individual's choice to undergo this procedure is based on the comparison of the risk to potential benefit. Although the majority of patients do not experience the following, you should discuss each of them with your physician to make sure you understand the risks, potential complications, limitations, and consequences of PLL tissue filler injections. Additional information may be obtained from the package-insert sheets supplied by the manufacturer.

Problems associated with the use of tissue fillers can relate to normal occurrences following tissue filler injections, or potential complications following tissue filler injections, including PLL tissue filler. Additional advisory information should be reviewed by patients considering tissue filler treatments that involve PLL tissue filler.

### Normal occurrences during tissue filler injections, including PLL Tissue Filler

Patients undergoing injections of PLL tissue filler may normally experience the following events:

**Bleeding and Bruising** - It is possible, though unusual, to have a bleeding episode from an injection or local anesthesia used during the procedure. Bruising in soft tissues may occur. Should you develop post-injection bleeding, it may require emergency treatment or surgery. Aspirin, anti-inflammatory medications, platelet inhibitors, anticoagulants, Vitamin E, Ginkgo biloba and other "herbs / homeopathic remedies" may contribute to a greater risk of a bleeding problem. Do not take any of these for seven days before injections. Bleeding and bruising can produce permanent tissue color changes.

**Swelling** - Swelling (edema) is a normal occurrence following the injections. It decreases after a few days. If swelling is slow to resolve, medical treatment may be necessary.

**Erythema (Skin Redness)** - Erythema in the skin occurs after injections. It can be present for a few days after the procedure.

**Needle marks** - Visible needle marks from the injections occur normally and resolve in a few days.

**Acne-like skin eruptions** - Acneiform skin eruptions can occur following the injection of tissue fillers. This generally resolves within a few days.

**Skin Lumpiness** - Lumpiness can occur following the injection of PLL tissue filler. This tends to smooth out over time. In some situations, it may be possible to feel the injected tissue filler material for long periods of time.

**Asymmetry** - The human face and eyelid region is normally asymmetrical in its appearance and anatomy. It may not be possible to achieve or maintain exact symmetry with tissue filler injections. There can be a variation from one side to the other in terms of the response to PLL tissue filler injection. This may require additional injections to improve your outcome.

**Pain** - Discomfort associated with tissue filler injections is normal and usually of a short duration. It is possible to have a fainting episode (vasovagal) from discomfort or anxiety about the injections.

### **Complications (adverse events)**

Potential complications attributable to the injection of soft tissue fillers, including PLL tissue filler:

**Infection** - Although infection following injection of tissue fillers is unusual, bacterial, fungal, and viral infections can occur. **Herpes simplex virus** infections around the mouth, can occur following a tissue filler treatment. This applies to both individuals with a past history of Herpes simplex virus infections and individuals with no known history of Herpes simplex virus infections in the mouth area. Specific medications must be prescribed and taken both prior to and following the treatment procedure in order to suppress an infection from this virus. Should any type of skin infection occur, additional treatment including antibiotics may be necessary.

**Damage to deeper structures** - Deeper structures such as nerves, blood vessels, and the soft tissues may be damaged during the course of injection. Injury to deeper structures may be temporary or permanent.

**Visible Tissue Filler Material** - It may be possible to see any type of tissue filler material that was injected in areas where the skin is thin.

**Skin Necrosis** - It is very unusual to experience death of skin and deeper soft tissues after PLL tissue filler injections. Skin necrosis can produce unacceptable scarring. Should this rare complication occur, additional treatments, or surgery may be necessary.

**Granulomas** - Painful masses in the skin and deeper tissues after a PLL tissue filler injection are extremely rare. Should these occur, additional treatments including antibiotics, injections, or surgery may be necessary. Granulomas may produce scarring within the skin and deeper structures.

**Allergic Reactions and Hypersensitivity** - It is unknown if PLL tissue filler is associated with serious systemic anaphylactic allergic reactions.

**Accidental Intraarterial injection** - It is extremely rare that during the course of injection, that tissue filler could be accidentally injected into arterial structures and produce a blockage of blood flow. This may produce skin necrosis in facial structures or damage blood flow to the eye, resulting in loss of vision. The risk and consequences of accidental intravascular injection is unknown and not predictable.

**Under/Over Correction** - The injection of soft tissue fillers to correct wrinkles and soft tissue contour deficiencies may not produce the desired outcome. The amount of correction may be inadequate or excessive. It may not be possible to control the process of injection of tissue fillers due to factors attributable to each patient's situation. If under correction occurs, you may be advised to consider additional injections of tissue filler materials. Over correction may require removal of tissue filler material.

## **Additional Advisories**

Advisories for patients considering semi-permanent tissue filler injections:

**Off-label usage of PLL** - PLL is labeled for specific use, the aesthetic treatment of nasolabial wrinkles and folds. The use of PLL for other conditions and disorders would be considered "off-label" usage by your physician. FDA defines off label use as, "Use for indication, dosage form, dose regimen, population or other use parameter not mentioned in the approved labeling." The FDA recognizes that off label use of drugs by prescribers is often appropriate and may receive endorsement from published literature. PLL may be used according to a physician's practice to treat other conditions.

**Unsatisfactory Result** - PLL tissue filler injections alone may not produce an outcome that meets your expectations for improvement in wrinkles or soft tissue depressions. There is the possibility of a poor or inadequate response. Additional injections may be necessary. Surgical procedures or other treatments may be recommended in addition to tissue filler treatments.

**Unknown Risks** - There is the possibility that additional risks and complications attributable to the use of tissue fillers may be discovered.

**Migration of Tissue Filler** - Product may migrate from its original injection site and produce visible fullness in adjacent tissue or other unintended effects.



**Drug and Local Anesthetic Reactions** - There is the possibility that a systemic reaction could occur from either the topical or local anesthetic or epinephrine used for sensory nerve block anesthesia when tissue filler injections are performed. This would include the possibility of light-headedness, rapid heart beat (tachycardia), and fainting. Medical treatment of these conditions may be necessary.

**Combination of Procedures** - In some situations, neurotoxin injections or other types of tissue filler materials may be used in addition to PLL tissue filler in order to specifically treat areas of the face or to enhance the outcome from tissue filler therapy. The effect of other forms of external skin treatments (laser and other light therapies, microdermabrasion, dermabrasion, or chemical peels) on skin that has been treated with tissue fillers is unknown. The effect of PLL tissue filler injections into tissue that has been formerly treated with other types of temporary or permanent tissue fillers is unknown.

**Pregnancy and Nursing Mothers** - Animal reproduction studies have not been performed to determine if PLL tissue filler could produce fetal harm. It is not known if PLL tissue filler or its breakdown products can be excreted in human milk. It is not recommended that pregnant women or nursing mothers receive tissue filler treatments.

**Drug Interactions** - It is not known if PLL tissue filler reacts with other drugs within the body.

**Long-Term Effects** - PLL tissue filler injections should not be considered as a permanent treatment for the correction of wrinkles and soft tissue depressions. Over time, the PLL tissue filler material is slowly absorbed by the body and replaced with collagen. Wrinkles or soft tissue depressions will reappear. Continuing PLL tissue filler treatment (injections) are necessary in order to maintain the effect. Subsequent alterations in face and eyelid appearance may occur as the result of aging, weight loss or gain, sun exposure, or other circumstances not related to tissue filler injections. Future surgery or other treatments may be necessary. Tissue filler injections do not arrest the aging process or produce permanent tightening of the skin or improvement in wrinkles.

## Health Insurance

Most health insurance companies exclude coverage for cosmetic surgical procedures and treatments or any complications that might occur from the same. Health insurance companies may not pay for tissue filler injections used to treat medical conditions. Please carefully review your health insurance subscriber information pamphlet.

## Additional Treatment Necessary

There are many variable conditions in addition to risk and potential complications that may influence the long-term result of PLL tissue filler injections. Even though risks and complications occur infrequently, the risks cited are the ones that are particularly associated with PLL tissue filler injections. Other complications and risks can occur but are even more uncommon. Should complications occur, additional surgery or other treatments may be necessary. You are advised to seek medical care should complications or adverse events occur after tissue filler treatments. Although good results are expected, there is no guarantee or warranty expressed or implied, on the results that may be obtained with the use of PLL tissue filler injections. The practice of medicine and surgery is not an exact science.

## Financial Responsibilities

This treatment provides a defined amount of PLL tissue filler for the treatment of wrinkles and other conditions. If additional interim injections of PLL or other tissue fillers are needed in order to maintain or improve results, you will be responsible for these costs in addition to the cost of this treatment session. It is unlikely that tissue filler injections to treat cosmetic problems would be covered by your health insurance. Additional costs of medical treatment would be your responsibility should complications develop from PLL tissue filler injections. You would also be responsible for additional forms of treatments or surgery recommended to improve the appearance of facial wrinkles and soft tissue depressions.

**In signing the consent for this surgery/procedure, you acknowledge that you have been informed about its risk and consequences and accept responsibility for the clinical decisions that were made along with the financial costs of all future treatments.**

## Disclaimer

Informed-consent documents are used to communicate information about the proposed treatment of a disease or condition along with disclosure of risks and alternative forms of treatment(s). The informed-consent process attempts to define principles of risk disclosure that should generally meet the needs of most patients in most circumstances.

However, informed consent documents should not be considered all-inclusive in defining other methods of care and risks encountered. Your physician may provide you with additional or different information which is based on all of the facts pertaining to your particular case and the state of medical knowledge.

Informed-consent documents are not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all of the facts involved in an individual case and are subject to change as scientific knowledge and technology advance and as practice patterns evolve.

**It is important that you read the above information carefully and have all of your questions answered before signing the consent on the next page.**

## CONSENT FOR SURGERY/PROCEDURE or TREATMENT

1. I hereby authorize Dr. \_\_\_\_\_ and such assistants as have been selected to perform the following procedure or treatment:

PLL TISSUE FILLER INJECTIONS: \_\_\_\_\_

I have received the following information sheet:  
INFORMED-CONSENT for PLL TISSUE FILLER Injection

2. I acknowledge that no guarantee has been given by anyone as to the results that may be obtained.
3. I consent to the administration of local anesthesia (regional nerve blocks, direct infiltration, or topical) to diminish discomfort of injection.
4. I consent to the photographing or televising of the operation(s) or procedure(s) to be performed, including appropriate portions of my body, for medical, scientific or educational purposes, provided my identity is not revealed by the pictures.
5. For purposes of advancing medical education, I consent to the admittance of observers to the treatment room.
6. IT HAS BEEN EXPLAINED TO ME IN A WAY THAT I UNDERSTAND:
- a. THE ABOVE TREATMENT OR PROCEDURE TO BE UNDERTAKEN
  - b. THERE MAY BE ALTERNATIVE PROCEDURES OR METHODS OF TREATMENT
  - c. THERE ARE RISKS TO THE PROCEDURE OR TREATMENT PROPOSED
  - d. THAT I ACCEPT RESPONSIBILITY FOR THE CLINICAL DECISIONS MADE ALONG WITH THE FINANCIAL COSTS OF ALL FUTURE TREATMENTS TO REVISE, OPTIMIZE OR IMPROVE OUTCOMES.

I CONSENT TO THE TREATMENT OR PROCEDURE AND THE ABOVE LISTED ITEMS (1-6). I AM SATISFIED WITH THE EXPLANATION THAT I HAVE RECEIVED BEFORE DECIDING TO UNDERGO THE TREATMENT OR PROCEDURE. I ACCEPT RESPONSIBILITY FOR THE RISKS, CONSEQUENCES, AND BENEFITS OF THIS DECISION.

\_\_\_\_\_  
Patient or Person Authorized to Sign for Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Witness

10-01-2010 version

**Does this version number  
on the bottom right need to appear?**

**If so, should all other forms now get a  
version number (which would be 2009)  
???**

# forms



- a. Injectable Order Form
- b. Neurotoxin Reconstitution Form
- c. Patient History and Treatment Female
- d. Patient History and Treatment Male
- e. BOTOX® Cosmetic Reconstitution Reference Sheet
- f. BOTOX® Cosmetic Administration Reference Sheet
- g. DYSPORT® Reconstitution Reference Sheet
- h. DYSPORT® Administration Reference Sheet

# safety with injectables™ order form



	Date Ordered	Ordered By:	#Vials Ordered	Injectable	Vendor	Confirmation #	Date Received	OK?
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								
18								
19								
20								

# safety with injectables™ neurotoxin reconstitution

Reconstitute BOTOX® Cosmetic 100 Unit vial with “X” ml of diluent = “XX” units per ml  
 Reconstitute DYSPORT® 300 unit vial with “X” ml of diluent = “XX” units per ml

	Date	Toxin Brand	Lot #	Vial Expiration date	Volume Diluent Added	Concentration units / ml	Expiration date reconstituted product	Name of individual who performed reconstitution
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								
18								
19								
20								

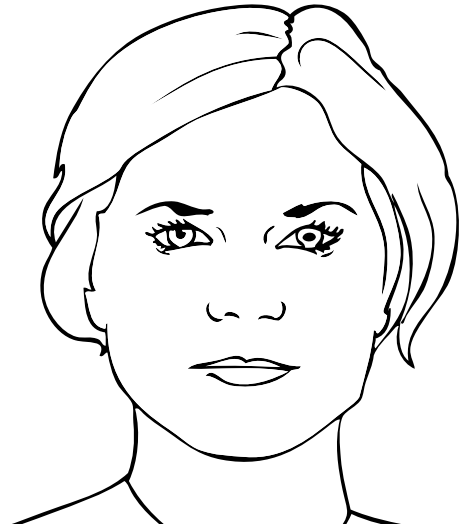
# patient history template female

## Patient History and Treatment (FEMALE)

Date: \_\_\_\_\_

Name: \_\_\_\_\_

Examination:



Medical History including prior cosmetic treatment / procedures: \_\_\_\_\_

Medications including ASA, NSAID, Herbs: \_\_\_\_\_

Allergies, including LATEX: \_\_\_\_\_

Treatment Plan: \_\_\_\_\_

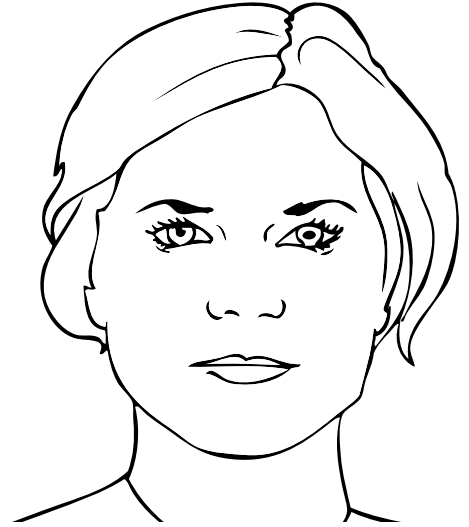
# patient history template female

>continued

## Injectable Treatment Template

Date: \_\_\_\_\_

Name: \_\_\_\_\_



Injectable(s): \_\_\_\_\_

Injectable labels/lot #'s: \_\_\_\_\_

Total Units/Volume: \_\_\_\_\_

Anesthesia: \_\_\_\_\_

Photography: \_\_\_\_\_

Comments: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Treatment provider: \_\_\_\_\_



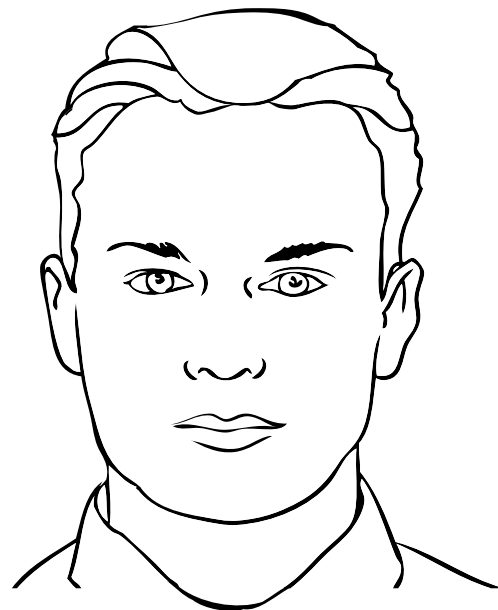
# patient history and treatment (male)

## Patient History and Treatment (MALE)

Date: \_\_\_\_\_

Name: \_\_\_\_\_

Examination:



Medical History including prior cosmetic treatment/procedures: \_\_\_\_\_

Medications including ASA, NSAID, Herbs: \_\_\_\_\_

Allergies, including LATEX: \_\_\_\_\_

Treatment Plan: \_\_\_\_\_

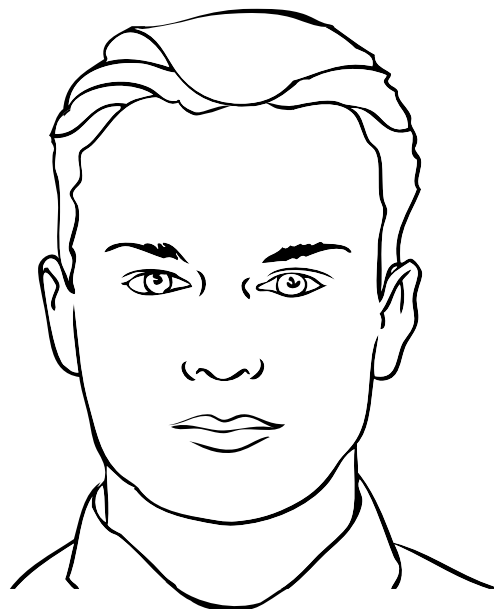
# patient history and treatment (male)

>continued

## Injectable Treatment Template

Date: \_\_\_\_\_

Name: \_\_\_\_\_



Injectable(s): \_\_\_\_\_

Injectable labels/lot #'s: \_\_\_\_\_

Total Units/Volume: \_\_\_\_\_

Anesthesia: \_\_\_\_\_

Photography: \_\_\_\_\_

Comments: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Treatment provider: \_\_\_\_\_

# botox<sup>®</sup> cosmetic (allergan) reconstitution reference



## Instructions For Reconstitution at XX Units/ml

### Reconstitution Protocol for BOTOX<sup>®</sup> Cosmetic at XX units/ ml

1. Verify that expiration date on BOTOX<sup>®</sup> Cosmetic package and vial is correct.
2. Follow Infection Control Procedure: Wash hands, sanitize work surface, use alcohol swab to disinfect top of diluent vial and 100 unit BOTOX<sup>®</sup> Cosmetic vial
3. With sterile technique draw up into a sterile syringe, XX ml of diluent
4. With sterile technique, add diluent to vial of 100 unit BOTOX<sup>®</sup> Cosmetic
5. Dispose of used syringe and needle as medical waste.
6. Write date of reconstitution, concentration (units), date of expiration on BOTOX<sup>®</sup> Cosmetic vial with Sharpie™ micro tip marker
7. Store reconstituted BOTOX<sup>®</sup> Cosmetic vial in refrigerator
8. Complete BOTOX<sup>®</sup> Cosmetic Reconstitution Log Form
9. Use reconstituted BOTOX<sup>®</sup> Cosmetic according to office policy and procedures



### Patient Safety Tips:

- > Do not leave needles/syringes inserted into vials- this is a direct route for microbial contamination of vial contents
- > Do not reuse needles, syringes, or gel cooling packs that have had patient contact (dispose as medical waste)
- > Never allow a needle/syringe that has had patient contact to be reinserted into the medication vial or IV bag/IV line
- > Never recap and store a partially-used syringe of injectable material for future use by the same patient
- > Medications should be discarded upon expiration or any time there are concerns regarding the sterility of the medication
- > Leftover parenteral medications should never be pooled for later administration

# botox<sup>®</sup> cosmetic (allergan) administration reference



**Corrugator:** “XX-XX” units in divided injections

**Procerus:** “XX-XX” units in divided injections

**Frontalis:** “XX-XX” units in divided injections\*

**Orbicularis, lateral (Crows Feet):** “XX-XX” units in divided injections\*

**Tail of lateral brow:** “XX-XX” units in divided injections\*

**Nasalis (bunny lines):** “XX-XX” units in divided injections\*

**Depressor Angularis Oris:** “XX-XX” units in divided injections\*

**Platysma:** “XX-XX” units in divided injections\*

**Other:** “XX-XX” units in divided injections\*

\*Disclose off-label usage

For Administration at XX Units/ml (On and Off-label)

## Administration Protocol for BOTOX<sup>®</sup> Cosmetic at XX units/ ml

1. Verify that expiration date on reconstituted BOTOX<sup>®</sup> Cosmetic vial is correct
2. Follow Infection Control Procedure: Wash hands, sanitize work surface, use alcohol swab to disinfect top of BOTOX<sup>®</sup> Cosmetic vial
3. With sterile technique draw up into a sterile syringe, BOTOX<sup>®</sup> Cosmetic, discard needle used for draw up and place needle for injection (30-32 gauge)
4. Perform injection of BOTOX<sup>®</sup> Cosmetic according to label or off-label.
5. Dispose of used syringe and needles as medical waste.
6. Complete patient treatment form regarding treatment areas, units used, lot number, etc.
7. Return reconstituted BOTOX<sup>®</sup> Cosmetic vial to refrigerator for storage



### Patient Safety Tips:

- > Do not leave needles/syringes inserted into vials- this is a direct route for microbial contamination of vial contents
- > Do not reuse needles, syringes, or gel cooling packs that have had patient contact (dispose as medical waste)
- > Never allow a needle/syringe that has had patient contact to be reinserted into the medication vial or IV bag/IV line
- > Never recap and store a partially-used syringe of injectable material for future use by the same patient
- > Medications should be discarded upon expiration or any time there are concerns regarding the sterility of the medication
- > Leftover parenteral medications should never be pooled for later administration

# dysport<sup>®</sup> (inosen-medicis) reconstitution reference



## Instructions For Reconstitution at XX Units/ml

1. Verify that expiration date on DYSPO<sup>®</sup> package and vial is correct.
2. Follow Infection Control Procedure: Wash hands, sanitize work surface, use alcohol swab to disinfect top of diluent vial and 300 unit DYSPO<sup>®</sup> vial
3. With sterile technique draw up into a sterile syringe, XX ml of diluent
4. With sterile technique, add diluent to vial of 300 unit DYSPO<sup>®</sup>
5. Dispose of used syringe and needle as medical waste.
6. Write date of reconstitution, concentration (units), date of expiration on DYSPO<sup>®</sup> vial with Sharpie<sup>™</sup> micro tip marker
7. Store reconstituted DYSPO<sup>®</sup> vial in refrigerator
8. Complete DYSPO<sup>®</sup> Reconstitution Log Form
9. Use reconstituted DYSPO<sup>®</sup> according to office policy and procedures



## Patient Safety Tips:

- > Do not leave needles/syringes inserted into vials- this is a direct route for microbial contamination of vial contents
- > Do not reuse needles, syringes, or gel cooling packs that have had patient contact (dispose as medical waste)
- > Never allow a needle/syringe that has had patient contact to be reinserted into the medication vial or IV bag/IV line
- > Never recap and store a partially-used syringe of injectable material for future use by the same patient
- > Medications should be discarded upon expiration or any time there are concerns regarding the sterility of the medication

# dysport<sup>®</sup> (ipson-medice) administration reference

**Corrugator:** “XX-XX” units in divided injections

**Procerus:** “XX-XX” units in divided injections

**Frontalis:** “XX-XX” units in divided injections\*

**Orbicularis, lateral (Crows Feet):** “XX-XX” units in divided injections\*

**Tail of lateral brow:** “XX-XX” units in divided injections\*

**Nasalis (bunny lines):** “XX-XX” units in divided injections\*

**Depressor Angularis Oris:** “XX-XX” units in divided injections\*

**Platysma:** “XX-XX” units in divided injections\*

**Other:** “XX-XX” units in divided injections\*

\*Disclose off-label usage

For Administration at XX Units/ml (On and Off-label)

## Administration Protocol for DYSPO<sup>®</sup> Cosmetic at XX units/ ml

1. Verify that expiration date on reconstituted DYSPO<sup>®</sup> vial is correct
2. Follow Infection Control Procedure: Wash hands, sanitize work surface, use alcohol swab to disinfect top of DYSPO<sup>®</sup> vial
3. With sterile technique draw up into a sterile syringe, DYSPO<sup>®</sup>, discard needle used for draw up and place needle for injection (30-32 gauge)
4. Perform injection of DYSPO<sup>®</sup> according to label or off-label
5. Dispose of used syringe and needle as medical waste
6. Complete patient treatment form regarding treatment areas, units used, lot number, etc.
7. Return reconstituted DYSPO<sup>®</sup> vial to refrigerator for storage



### Patient Safety Tips:

- > Do not leave needles/syringes inserted into vials- this is a direct route for microbial contamination of vial contents
- > Do not reuse needles, syringes, or gel cooling packs that have had patient contact (dispose as medical waste)
- > Never allow a needle/syringe that has had patient contact to be reinserted into the medication vial or IV bag/IV line
- > Never recap and store a partially-used syringe of injectable material for future use by the same patient
- > Medications should be discarded upon expiration or any time there are concerns regarding the sterility of the medication
- > Leftover parenteral medications should never be pooled for later administration

## Introduction

The use of cosmetic injectables offers much to patients and provides a unique economic sustainability to practices. Much of this comes down to having a strategy within the practice to manage this unique opportunity of provide patients with a service that delivers high satisfaction and, at the same time, excellent revenue for the practice.

All of this is somewhat contingent on the presence of policies and procedures for the use of injectables along with a business process to capture revenue that injectables will produce.

The safe (and effective) use of cosmetic injectables is in reality a series of connected events, otherwise called a process. The same applies to the business side of the matter. If one looks at the entire process from a holistic perspective, it becomes straightforward to develop your own way of using cosmetic injectables as an integral part of the services that you offer and part of your practice's business model.

## Service Mapping and Process Development

The process for the use of injectables is far more complex than just sticking a needle into a patient to administer an injectable and swiping their credit card for payment. There are many requisite steps that occur on two levels.

First, there are the interactions that occur when a patient goes to your web site or calls to seek information regarding injectables. From this point onward, it is possible to construct a service map of their experience until they are treated, leave the office and then return for additional treatments with cosmetic injectables (or even surgery).

The second component of the process relates to how you develop the business model for the profitable use of injectables, inventory control, and accounting for what each patient received. Within an active cosmetic medicine practice, there are literally hundreds of items that are used each month, ranging from cosmetic injectables, skin care products, and other non-invasive light-based treatments (and the ensuing staff time for their administration). All of these require both administration and accounting.

The emphasis of this chapter focuses on the individual practice working to develop a process for the effective use of cosmetic injectables and the corresponding business model. Both of these are interrelated and necessary. Alternatively, there may be a revenue loss if product and services are not accounted for and appropriately charged to patients.

To start, you may want to close the office for an afternoon and work with your staff to develop a service map of how you want to use injectables. This is even relevant for practices that are using cosmetic injectables already, as there most likely are broken processes in place and waste (including revenue leaks) that occurs.

Spend this time with staff to develop a map of how we use cosmetic injectables and

the business model of ordering, accounting, and revenue collection in order to surround ourselves with a process for their use. From this, one can generate a profit/loss statement for the revenue that cosmetic injectables produce. The business literature is replete with books and articles on production systems, such as the one developed by Toyota (Toyota Production System) and Lean Manufacturing<sup>1</sup>. In essence, these approaches are designed to allow for continuous innovation to improve a process, to reduce waste, and to mistake-proof work.

Within the service mapping exercise, ask staff some basic questions that relate to what resources are needed at each step of the process, what are the fail points that could go wrong, and what would they do to improve the process. As one can imagine, it is possible to look at each step in many different levels, from how the telephone is answered when a patient calls, to the quality of material on your practice's web site, to what specific materials you have internally developed regarding injectables. There are also periodic promotions that manufacturers offer for the use of injectables that can be very powerful incentives for patients.

Service mapping allows the staff to visualize the entire process as a series of interconnected steps and recognize their role in the process. It also gives them opportunity to “own” their part of the process and to innovate versus being disconnected. Staff performance is generally enhanced when they have a better understanding of the complete process.

Service mapping also applies to the business of injectables. Within your office, consider adopting the position that injectables are drugs and that their use must be accounted for. The process of ordering, inventory, administration, and revenue capture should be defined within the business model of the practice. Injectables are expensive items that are used in volume; they must be accounted for within a practice in order to prevent revenue leaks. Even in situations where injectables are given on a complimentary basis as part of a bundled facial rejuvenation procedure, their use is logged. Injectables administered to staff must be accounted for in the record.

Service mapping exercises represent great opportunities to define a process and to innovate. The Second Edition of the workbook includes an “injectable passport” for each patient that contains information regarding what injectable they received and when it was administered. The “passport” provides useful top-level information versus having to look through multiple treatment templates.

The second template is used to allocate which patient received what injectable. This can

<sup>1</sup> <http://www.ihl.org/IHI/Results/WhitePapers/GoingLeaninHealthCare.htm>



be as simple as a tabbed 3-ring binder with individual categories for injectables. Each time fillers or neurotoxins are administered, an entry is made in the applicable section. From this, it's possible to audit injectable usage and reconcile with inventory.

This concept can be adapted to an Excel® spreadsheet if you want to keep it electronically and use the advanced functions of Excel® to assist with inventory control, etc. Other advanced accounting approaches would involve barcodes and scanners that are supported by practice management and other business programs.

One of the other benefits of service mapping is in reducing waste. Within this context, waste would be defined as excessive back and forth staff movements during the process of injectables. When you think about it, there are many ways to be more efficient with injectables in terms of scheduling, how you administer the injection, and what the requisite steps for staff are before the doctor even sees the patient, such as photography, giving the patient the treatment consent to read, applying the topical anesthetic cream, etc.

## Chapter Summary

The effective use of cosmetic injectables requires both an understanding of the human factors that involve patients seeking improvement and the knowledge of what it takes to deliver patient satisfaction. This relates to having a process that physician and staff can trust to deliver excellent, safe outcomes in an efficient, business-like fashion. Patients are looking for a process that they can trust to meet their expectations for improvement with cosmetic injectables, other non-invasive treatments (medical skin care, light-based treatments, etc.) or aesthetic surgery. The impact of cosmetic injectables in the business model of aesthetic surgical practices will only continue to grow in the future. It is essential that this opportunity be well-managed in order that it produces long-term financial profitability and practice sustainability.

## The Business of Injectables

Many clinics have been traditionally oriented towards the episodic billing for services and supplies, primarily to 3rd party insurers. Until the last few years, there was not an ability to account for inventory or point of sales activity within practice management software programs. Currently, many offices sell cosmeceuticals, injectables, and bill for spa services. This has allowed the non-surgical component of revenue to be better managed.

Office policy and procedure need to be designed to account for the use of injectables, just like any other drug or supply that is sold to patients. A business system must be designed to follow an injectable product from ordering to receipt of shipment into inventory and then on to which patient received it. Similarly, free product that is received for promotion or staff

use must be accounted. The goal of this approach is to prevent loss of revenue from poor accounting practices or employee theft of injectables.

I have found it useful to have a notebook that is next to the locked cabinet where injectables are stored that contains tabbed divider pages for the different categories of injectables. It is really easy to allocate injectables and reconcile inventory. This includes the free-of-charge use of injectables for staff and occasional patient touch up at the discretion of the physician.

Other approaches that use barcodes and scanners may be considered for injectable inventory, allocation, and revenue capture. These may be more involved to develop and implement, but should be considered for clinics that consume a large volume of injectables.

## Summary

Cosmetic medicine offers practices the opportunity for substantive financial growth and increased cash flow revenues over a traditional surgery-only orientation. The effective and profitable use of injectables depends on each clinic designing a process that delivers operational excellence, including an accounting for how each injectable was administered and billed. It is in this way that profitability is maximized and revenue leaks are minimized.

## References:



# the business of injectables

>continued

## Allocation

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