## Test your knowledge on stability

### Table of incompatibilities: A new function in Stabilis®

### News from congresses

- News from the ASHP Midyear Meeting
- News from the APHIF Congress
- News from the ESOP / DGOP Congress

### A visit to Loccioni company, Ancona, Italy

### The new Trissel’s handbook available

### First ESOP Webinar

### New monographs

- Oritavancin, Blinatumomab, Vincristine sulfate liposome, Ramucirumab, Siltuximab, Pembrolizumab, Omacetaxine mepesuccinate

### New references from international publications

- Alprostadil, Ceftazidime - Cefazolin, Dexrazoxane, Ifosfamide - Mesna, Melphalan, Metoclopramide - Diphenhydramine - Dexamethasone, Paracetamol, Phenylephrine, Obinutuzumab

### New documents on Infostab website

## Statistics

Focus on Vietnam

Answer to the test
News from
the APHIF Congress

The Congress of APHIF was organized in Paris in November 2014. We have selected one poster about the physico chemical compatibility of phloroglucinol.

Phloroglucinol is used as a treatment for gallstones, spasmodic pain and other related gastrointestinal disorders. It has a non-specific spasmolytic action on the vessels, bronchi, intestine, ureters and gall bladder, and is used for treating disorders of these organs. It is the main ingredient of the drug Spasfon®, available in France, where it is one of the most sold drugs.

Test your knowledge on stability!

Which analytical methods can be used to detect aggregation of proteins?

- Size exclusion chromatography
- Ionic chromatography
- Dynamic light scattering
- Capillary electrophoresis
- Peptide Mapping

See the answer on the last page.

Table of incompatibilities: A new function in Stabilis®

In medical wards where many injectable drugs are used, the problem of the potential incompatibilities during administration has to be tackled in the daily practice. Most of the incompatibilities between the drugs have precipitation as a consequence. If these non soluble particles enter into the veins of the patients, they can cause serious medical problems like embolism.

The incompatibilities can be checked in Stabilis® by using, in the monographs, the button «Incompatibilities» or by using the «search function for incompatibilities».

However, it can be interesting for the nurses in the medical wards like «Oncology unit», «Hematology unit» or «Intensive care unit» to have a synthetic and personalized information about the potential incompatibilities which can occur with the main injectable drugs used in the daily practice.

For this purpose, a new function has been created in Stabilis®. The Stabilis® user has now the possibility to create his own table of incompatibility: a new button «Table of incompatibility» has been added on the left side of the screen. By clicking on this button, the user will obtain the screen presented below. He has to enter the name of his hospital, the name of the medical ward and then to select the injectable drugs commonly used in the daily practice. By clicking on «Confirm entry», a personalized «Incompatibility table» will be created (see the example below) and can be printed in A3 format or as a poster.
News from the ESOP / DGOP Congress

The meeting of the ESOP delegates of the European Society of Hospital Pharmacists was organized with the DGOP (German Society of Oncology Pharmacists) like each year at the Lindtner Hotel in Hamburg, Germany.

The conference room at the Lindtner Hotel, Hamburg

The «Quapos 5, Quality Standard for the Oncology Pharmacy Service» was presented. This book contains a chapter «Stability of the preparations». It can be ordered on the website of the ESOP: http://www.esop.li/activities.php

News from the ASHP Midyear Meeting

The 49th ASHP Midyear Clinical Meeting took place in Anaheim, California, December 7-11, 2014.
4 posters were about stability and compatibility

1-Extended stability of reconstituted chlorothiazide vial.
Moore W, Cees J, Mason R.
2-Development of a quick reference guide for syringe driver drug compatibilities.
McCabe L, Kehoe B, Conlon L, Meegan C.
3-Extended stability of chlorothiazide vial reconstituted with bacteriostatic water for injection.
Wayne Moore et al.

4-Pharmacy based preparation and stability of ready-to-administer epinephrine injection solution (0.02 mg/ml, 50 ml)
Reichhold J, Heeb R.M, Krämer I.
Universitätsklinikum Mainz, Germany.
See in «New documents on Infostab website»
The stability study has been performed by HPLC with UV detection at 280 nm. The conclusion was that physicochemical stability is given over at least six months under refrigerated storage conditions.

The Anaheim Convention Center. (Photo credit: Anaheim-Orange County Image Library)

A visit to Loccioni company

Loccioni is an Italian company located in Ancona which is involved in many activities related to innovation, automation and measure, including the development of robots for the preparation of chemotherapy. The system is called «APOTECACHemo».

The stability is a key point in the production of cytotoxic infusions and the possibility to use the Dose Banding concept with the robot is a topic of interest for APOTECACHemo community, the international scientific network of users of APOTECACHemo.

The «Story of Stabilis®» was presented during a meeting on February 11th in Ancona. The story of the database since the first idea in 1997, the first CDROM in 2001 and the opening of the website in 2008 until the new function «table of incompatibility», announced in this newsletter, were presented to the audience.
Then we visited the chemotherapy production in Ancona University Hospital with Celestino Bufarini (Head of Oncology Pharmacy) and the Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRCCS - I.R.S.T in Meldola with Carla Masini (Director of Pharmacy).

Discussion about stability studies with the team of the IRST in Meldola.

A group picture with the Loccioni team and Italian hospital pharmacists!

First ESOP Webinar

On March 11th 2015 the European Society of Oncology Pharmacy (ESOP) organized the first Webinar to present Stabilis®.

The maximum of 100 participants was quickly reached. Participants came from 21 countries (By alphabetical order : Algeria, Belgium, Canada, Cyprus, Egypt, France, Germany, Iceland, Italy, Japan, Latvia, Macedonia, Morocco, Pakistan, Poland, Portugal, Saudi Arabia, Serbia, Spain, Tunisia, Turkey).

This webinar was used to present the story of the creation of the database and all the functions of Stabilis. Many thanks to Klaus Maier, president of ESOP and Ahmet Bosnak and his team for organizing this conference.

The new Trissel’s Handbook available

The 18th edition brings together information on parenteral drugs available in the United States and in other countries in 338 drug monographs. About 50% of the monographs have been revised and updated for this edition to include new drugs, expanded and updated stability and compatibility information, more specific referencing of manufacturer information, and other enhancements.

See on the website of ASHP: [www.ashp.org/handbook18](http://www.ashp.org/handbook18)
New monographs

**Oritavancin**

Oritavancin (Orbactiv®) is a novel semisynthetic glycopeptide antibiotic being developed for the treatment of serious Gram-positive bacterial infections.

Preparations of Oritavancin 1,32 mg/ml diluted with 5% dextrose injection are stable for up to 12 hours when refrigerated and for 6 hours at room temperature.

Normal saline for dilution is incompatible with Oritavancin.

*Summary of Product Characteristics, the Medicines Compagny 2012*

**Blinatumomab**

Blinatumomab (Blincyto®) combines two binding sites: a CD3 site for T cells and a CD19 site for the target B cells.

Polyolefin, PVC non di-ethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags/pump cassettes must be used for the preparation of Blinatumomab.

Reconstituted Blinatumomab 12,5 µg/ml vials are stable 4 hours at 23-27°C and 24 hours at 2-8°C. Prepared IV bags containing Blinatumomab solution for infusion are stable 48 hours at 23-27°C and 8 days at 2-8°C.

*Summary of Product Characteristics, Amgen 2014*

**Ramucirumab**

Ramucirumab (Cyramza®) is a human vascular endothelial growth factor receptor 2 antagonist, indicated

- as a single agent or in combination with paclitaxel, for treatment of advanced gastric or gastro-esophageal junction adenocarcinoma if the disease has progressed despite fluoropyrimidine- or platinum-containing chemotherapy.

- in combination with docetaxel, for treatment of metastatic non-small-cell lung carcinoma with disease progression on or after platinum-containing chemotherapy. If the cancer has a sensitizing mutation of EGFR or ALK, previous therapy should have included targeted therapy for the genomic tumor aberration.

The infusion solution of Ramucirumab must be prepared in 0.9% sodium chloride injection. Dextrose containing solutions must not be used. Diluted infusion can’t be stored for more than 24 hours at 2-8°C or 4 hours at room temperature.

*Summary of Product Characteristics, Eli Lilly 2014*

**Vincristine sulfate liposome**

Vincristine is a mainstay of treatment of hematologic malignancies and solid tumors due to its well-defined mechanism of action, demonstrated anticancer activity and its ability to be combined with other agents. Vincristine sulfate liposome (Marqibo®) was developed to increase the circulation time, optimize delivery to target tissues and facilitate dose intensification without increasing toxicity.

Marqibo® is indicated for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following 2 or more anti-leukemia therapies.

Solutions of 0.16 mg/ml of Vincristine sulfate liposome in glass vial are stable when stored at 15-30°C during 12 hours. After transfer in an infusion bag containing of 0.9% sodium chloride injection or 5% dextrose injection, the solution may be stored at 15-30°C during 12 hours.

*Summary of Product Characteristics, Talon Therapeutics 2012*
Siltuximab
Siltuximab (Sylvant®) is a chimeric (made from human and mouse proteins) monoclonal antibody. It binds to interleukin-6.
Siltuximab is indicated for the treatment of patients with multicentric Castleman’s disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.
Infusion bags (250 ml) must contain dextrose 5% in water and must be made of polyolefin or PVC with di-ethylhexylphtalate (DEHP).
The reconstituted product should be kept for no more than 2 hours prior addition into the infusion bags. The infusion should be completed within 4 hours of the dilution of the reconstituted solution to the infusion bag.
*Summary of Product Characteristics, Janssen Biotech 2014*

Pembrolizumab
Pembrolizumab (Keytruda®) is a human programmed cell death receptor 1 (PD-1) blocking antibody, indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.
The final concentration of the diluted solution should be between 1 to 10 mg/ml. Diluted solutions in 0.9% sodium chloride injection are stable for no more than 4 hours at room temperature and 24 hours under refrigeration.
*Summary of Product Characteristics, Merck Sharp & Dohme 2014*

Omacetaxine mepesuccinate
Omacetaxine mepesuccinate (Synribo® or Myelostat®) is indicated for the treatment of adult patients with chronic myeloid leukemia with resistance and/or intolerance to two or more tyrosine kinase inhibitors. It is a natural ester of the alkaloid cephalotaxine from Cephalotaxus harringtonia, manufactured by hemi-synthesis.
Omacetaxine mepesuccinate (Synribo®) diluted to 3,5 mg/ml with 0.9% sodium chloride injection is stable for 12 hours at room temperature and 24 hours under refrigerated.
*Summary of Product Characteristics, Teva Pharmaceuticals 2014*

New references from international publications

**Stability of injectable drugs**

**Alprostadil**
Preparations of Alprostadil 1.5 or 15 µg/ml diluted with 10% dextrose are stable for up to 48 hours when stored in polypropylene syringes at 28-32°C.
*Pharmacist Master, University of Genève 2014*

**Ceftazidine - Cefazolin**
Premixed ceftazidime and cephazolin in a 7.5% icodextrin or pH neutral PD solution are stable for at least 168 hours when refrigerated. Both the antibiotics are stable for at least 24 hours at 25 and 37°C.
*Perit Dial 2014 ;34:212-218*

**Dexrazoxane**
Reconstituted dexrazoxane solutions further diluted to 1 or 3 mg/ml solutions are stable for at least 24 h and 8 h respectively, in PVC bags at room temperature.
*J Oncol Pharm Pract 2014 ;20,1:58-64*

**Ifosfamide - Mesna**
The mixture Ifosfamide with Mesna in 1:1 combination at 10, 20 and 30 mg/ml is physicochemically stable for 14 days at room temperature in PVC bags.
*J Oncol Pharm Pract 2014 ; 20, 1: 51-57*

**Melphalan**
Melphalan reconstituted and diluted to 300 µg/ml can be stored at -20°C for 6 months without loss of significant amounts of the drugs.
*JAMA Ophtalmology 2014 ;132,11:1372*
Metoclopramide – Diphenhydramine - Dexamethasone
An IV admixture containing metoclopramide 1.6 mg/ml, diphenhydramine hydrochloride 2 mg/ml and dexamethasone sodium phosphate 0.16 mg/ml in 0.9% sodium chloride injection was chemically stable for 48 hours when stored at room temperature without light protection.

Paracetamol
Acetaminophen >1 mg/ml is stable at room temperature for at least 48 hours in 0.9% sodium chloride injection or 5% dextrose infusion.
Summary of Product Characteristics, B Braun

Phenylephrine
Phenylephrine hydrochloride (Vazculep®) diluted to 20 or 100 µg/ml with normal saline or 5% dextrose is stable for 4 hours at room temperature and 24 hours under refrigerated.
Summary of Product Characteristics, Eclat Pharmaceuticals

Obinutuzumab
After dilution, chemical and physical stability of Obinutuzumab (Gazyvaro®) have been demonstrated in 0.9% sodium chloride solution for injection at concentrations of 0.4 to 20 mg/ml for 24 hours at 2-8°C followed by 48 hours (including infusion time) at <30°C.
Summary of Product Characteristics, Roche Products 2014

New references of incompatibility
- Incompatibility of Amiodarone with sodium bicarbonate, furosemide, heparine and thiopental (Enferm Clinica 2014; 21,1).
- Incompatibility of Sodium bicarbonate with amiodarone, cisatracurium, haloperidol, midazolam and thiopental (Enferm Intens 2011; 22,2).
- Incompatibility of Furosemide with amiodarone, cisatracurium, haloperidol, midazolam and urapidil (Enferm Intens 2010; 21,3).

Stability of oral solution

Stability of Extemporaneously Compounded Clonidine in Glass and Plastic Bottles and Plastic Syringes
Ensom M.H.H, Décarie D.
The purpose of the current study was to evaluate whether extemporaneously prepared clonidine suspensions (0.010 mg/mL) are physically and chemically stable in other commercially available vehicles, specifically Oral Mix® and Oral Mix SF®. All suspensions were easily resuspended, with no notable changes in the milky white color; the faint, tart cherry taste; or odor during the study period. HPLC analysis showed that all suspensions maintained more than 94% of the original concentration for 91 days. Also, clonidine suspensions (0.010 mg/mL) in Oral Mix and Oral Mix SF stored in amber glass bottles, plastic bottles, or oral plastic syringes at 25°C or in amber glass or plastic bottles at 4°C can be expected to remain stable for up to 91 days.

Stability of cilazapril in pediatric oral suspensions prepared from commercially available tablet dosage forms
Beta J. Stanisz, Sylviak. Paszun and Anna Zalewska
Cilazapril oral suspensions at concentration of 1 mg/mL demonstrated satisfactory stability over 28 day long storage at room temperature. Cilazapril concentrations remained within acceptable limit (± 10%) stored in closed amber bottles made of glass or amber plastic PET bottles. Moreover, suspensions physical properties remained unaffected. Cilazapril - Ora-Blend® pediatric oral liquid is easy to made, palatable and stable when stored at room temperature for 28 days. Stability of cilazapril oral liquid remains unchanged while using cilazapril tablets produced by different manufacturers and bottles made of amber glass or PET material.

Stability of Extemporaneously Compounded Pyridoxine in Glass and Plastic Bottles and Plastic Syringes
Ensom M.H.H, Décarie D.
The purpose of the current study was to evaluate whether pyridoxine suspensions (25 mg/mL) are physically and chemically stable in commercially
available vehicles, specifically Oral Mix® and Oral Mix SF®. Stock pyridoxine suspensions (25 mg/mL) were prepared by diluting pyridoxine hydrochloride 100 mg/mL for injection in Oral Mix® and Oral Mix SF®.

HPLC analysis showed that all pyridoxine suspensions maintained at least 94.2% of original concentrations for 91 days. In conclusion, pyridoxine suspensions (25 mg/mL) in Oral mix® and Oral Mix SF® suspension vehicles stored in amber glass bottles, plastic bottles, or oral plastic syringes at 25°C or in amber glass or plastic bottles at 4°C can be expected to remain stable for up to 91 days.


New documents on Infostab website

www.infostab.com
See in « Publications » and « Stability and compatibilities »

1. Reichhold J., Heeb R. M., Krämer I.
Pharmacy based preparation and stability of ready-to-administer epinephrine injection solution (0.02 mg/mL, 50 mL)
Department of Pharmacy – University Medical Center of the Johannes Gutenberg University, Mainz, Germany
Poster presented at the 49th ASHP midyear clinical meeting, Anaheim, California, December 2014

Étude de la compatibilité physico-chimique du phloroglucinol injectable durant les mélanges au sein des tubulures en Y.
Pitié Salpêtrière University Hospital, Paris
Poster presented at the Aphif Congress, Paris, France, November 2014

Statistics

Languages

No change this time: let’s see in the future how new languages evolve!

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As promised in our last newsletter, here is the frequention of Stabilis website since 2008. All efforts of the team to improve the website and the database (languages, routes of administration, level of evidence...) have been rewarded by our visitors. Thank you all: we'll keep on providing you with new features!

Statistics since the opening of Stabilis in February 2008.

Country focus: Vietnam

For this newsletter we have decided to highlight our colleagues from Vietnam. The recent months have seen a great rise in Stabilis frequention: thank you!
Answer to the test

- Size exclusion chromatography
- Dynamic light scattering
- Peptide Mapping

- Ionic chromatography
- Capillary electrophoresis

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