

BRIEF REPORT

Thermolabile Drugs. Operating Procedure in the Event of Cold Chain Failure[☆]

L. Periañez Parraga,^{*} A. Gómez-Lobón, I. Gamón Runnenberg,
R. Seco Melantuche, O. Delgado Sánchez, F. Puigventós Latorre

Servicio de Farmacia, Hospital Universitario Son Dureta, Palma de Mallorca, Mallorca, Spain

Received 7 May 2010; accepted 15 July 2010

Available online 21 October 2011

KEYWORDS

Drug stability;
Drug storage;
Refrigeration;
Cold chain

Abstract

Objective: To establish a standard operating procedure in the event of cold chain failure.

Method: We selected thermolabile drugs included in the hospital's pharmaceutical guide. We performed a review of the available literature, classifying each drug into a given category with an intervention protocol for each one.

Results: We reviewed 254 drugs (162 active ingredients). Categories were: A (stable ≥ 28 days at 25 °C): 65 drugs; B (≥ 7 days at 25 °C): 47 drugs; C (≥ 48 h at 25 °C): 30 drugs; D (<48 h at 25 °C): 47 drugs; E (unstable > 8 °C): 12 drugs; F (batch-dependent) 22 drugs. Thirty-one drugs were not classified into any category.

The intervention protocol consisted of establishing a system to monitor the products concerned, and discarding or returning them to the laboratory if they were to exceed the time or temperature limit indicated for each category.

Discussion: The aim of this study is to make intervention quicker in the event of cold chain failure.

© 2010 SEFH. Published by Elsevier España, S.L. All rights reserved.

PALABRAS CLAVE

Estabilidad;
Conservación
de fármacos;
Refrigeración;
Cadena de frío

Medicamentos termolábiles. Protocolo de actuación en la rotura de la cadena de frío

Resumen

Objetivo: Establecer un procedimiento normalizado de trabajo en caso de rotura de cadena de frío.

Método: Se seleccionaron los medicamentos termolábiles incluidos en la guía farmacoterapéutica del hospital y se revisó la bibliografía disponible, clasificándolos en categorías con un protocolo de actuación en cada caso.

[☆] Please cite this article as: Periañez Parraga L, et al. Medicamentos termolábiles. Protocolo de actuación en la rotura de la cadena de frío. Farm Hosp. 2011;35(4):190.e1–190.e28.

^{*} Corresponding author.

E-mail address: leonord.perianez@ssib.es (L. Periañez Parraga).

Resultados: Se revisaron 254 medicamentos (162 principios activos). La distribución por categorías fue: A (estable ≥ 28 días a 25°C): 65 medicamentos; B (≥ 7 días a 25°C): 47; C (≥ 48 h a 25°C): 30; D (< 48 h a 25°C): 47; E (no estable $> 8^{\circ}\text{C}$): 12; F (depende del lote): 22. No se clasificaron en ninguna categoría 31 medicamentos.

El protocolo de actuación consistió en establecer un sistema de seguimiento de los medicamentos afectados y desechar o devolver al laboratorio en caso de superarse el límite de tiempo o temperatura establecido en cada categoría.

Discusión: El trabajo realizado pretende facilitar la rápida actuación en aquellas situaciones de rotura de la cadena de frío.

© 2010 SEFH. Publicado por Elsevier España, S.L. Todos los derechos reservados.

Introduction

The cold chain is the set of logistical links that guarantee that a temperature between 2°C and 8°C is maintained during the processes of storage, handling, transport and distribution of drugs. If this is not done, drug properties are liable to change in varying degrees, depending on the temperature reached and the time spent at that temperature.

There are procedures for receiving, storing and distributing drugs in hospitals to ensure that the cold chain is maintained. Standard operating procedures and facilities ensure that the proper temperature is maintained. The complexity of drug distribution processes in hospitals means that there are cold storage facilities available in a large number of locations in the pharmacy department storage areas, as well as the drug storage areas of inpatient units, day hospitals, operating rooms and outpatient clinics, among others.

The cold chain may be broken in many unexpected ways during daily practice (e.g., due to a power failure, cold room breakdowns, inadequate transportation or an error in storage conditions). These incidents may affect just a few units of a drug in a hospital ward or may affect complete clinical containers due to a refrigerator failure.

Administering a drug which has been inadequately stored can have highly variable potential consequences for the patient. Some medications are affected by a temporary and an isolated break in the cold chain: a number of drugs may lose some efficacy of little clinical relevance, while others may have a total loss of activity or may even become toxic.¹

In addition, a break in the cold chain may have a significant economic impact for the hospital if the full activity of a drug cannot be guaranteed and it has to be disposed of, and there were no conditions established for its return to the pharmaceutical company supplying it.

The potential clinical and economic impacts posed by the loss of this group of drugs make it necessary to have a protocol for maintaining the cold chain and establishing actions if it is broken. This includes a drug stability report, including the time and temperature to which the drug has been exposed. It is also important to provide information about any such event, as affected batches will have to be withdrawn, and it is important to know whether they can be used or not.

The aim of this study was to establish a standard procedure for a break in the cold chain, prepare an updated list

(to 2010) on the maximum stability of thermolabile active ingredients at room temperature, classify them according to the possibility of re-using them for certain time periods and provide a communication system on the hospital intranet and via the Internet.

Method

The main active ingredients to be kept at a temperature between 2°C and 8°C or in the freezer were selected from the hospital pharmacotherapeutic guide.

A review of previously published studies in PubMed with the MESH Drug Stability, Drug storage, refrigeration and Cold chain was carried out.²⁻¹⁰ The information available from the summaries of product characteristics (SmPCs) was taken and the pharmaceutical manufacturer was consulted by fax or e-mail if there was any doubt or lack of data.

An Excel table was prepared, which included speciality-specific data, bibliographic references, and the contact details of the pharmaceutical company department, where appropriate.

Table 1 Classification of Drugs.

| Category | Stability | Action |
|----------|--------------------------------------------------------------|---------------------------------------------------------------------|
| A | Stable ≥ 28 days at 25°C | Label if it meets the conditions. If not, discard |
| B | Stable ≥ 7 days and < 28 days at 25°C | Label if it meets the conditions. If not, discard |
| C | Stable ≥ 48 h and < 7 days at 25°C | Label if it meets the conditions. If not, discard |
| D | Stable < 48 h at 25°C | Evaluate individually depending on the time and temperature reached |
| E | Not stable outside the fridge ($> 8^{\circ}\text{C}$) | Discard |
| F | Stability depends on the batch | Consult laboratory |

Table 2 Recommendations After Breaking the Cold Chain.

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|-------------------|---------------------------------|-------------------------------|--------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-------------------------|----------|
| Abciximab | Reopro® vial 50 mg/ml | Lilly | 8 days at 28 °C (192 h) | Consult lab 28/07/09 | 916635000 | B |
| Carglumic acid | Carbaglú® 200 mg tablets | Orphan Europe | 1 month at <30 °C | SmPCs (2003) | | A |
| Adalimumab | Humira® 40 mg prefilled syringe | Abbott Laboratories | 8 h | Cobos Campos et al., 2006 ³ | | D |
| Agalsidase alfa | Replagal® 3.5 mg vial | Shire Human Genetic Therapies | 24 h | SmPCs (2006) | | D |
| Alemtuzumab | MabCampath® 30 mg vial | Bayer Healthcare | 7 days at 25 °C | Consult lab 20/2/09 | 934956500 | B |
| Alfacalcidol | Etalpha® ampoules 1 mcg | Leo Pharma | 1 year at 25 °C | Bovaira García et al., 2004 ⁴ | 932213366 | A |
| Alfacalcidol | Etalpha® ampoules 2 mcg | Leo Pharma | 1 year at 25 °C | Bovaira García et al., 2004 ⁴ | 932213366 | A |
| Alfacalcidol | Etalpha® drops | Leo Pharma | 1 year | Consult lab 16/02/09, Bovaira García et al., 2004 ⁴ | 932213366 | A |
| Alprostadil | Alprostadil® 500 mcg/ml | Pfizer | 4 months | Cuervas-Mons et al., 2004, ⁶ García Vázquez et al., 1997 ⁷ | | A |
| Alteplase | Actilyse® 20 mg | Boehringer Ingelheim Spain | 3 years at <25 °C | Bovaira García et al., 2004 ⁴ | | A |
| Alteplase | Actilyse® 50 mg | Boehringer Ingelheim Spain | 3 years at <25 °C | Bovaira García et al., 2004, ⁴ Cuervas-Mons et al., 2004 ⁶ | | A |
| Amphotericin B | Abelcet® 50 mg vial | Cephalon Pharma | 1 day outside fridge = 9 days in fridge (change expiry date) | Cobos Campos et al., 2006 ³ | Specific recommendation | |
| Amphotericin B | Fungizona® 50 mg vial | Bristol Myers Squibb | 2 weeks-1 month | Cuervas-Mons et al., 2004 ⁶ Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004 ⁶ | | B |
| Digoxin antidote | Digitalis Antidot® 80 mg vial | Roche Farma Farma | 20 days up to 40 °C | Silgado et al., 2006 ² | | B |
| Asparaginase | Erwinase® (ME) 10,000 IU vial | Opi | 2 years | García Vázquez et al., 1997 ⁷ | | A |
| Asparaginase | Kidrolase® 10,000 IU vial | Opi | 48 h (1), 7 days (2) | Cuervas-Mons et al., 2004 ⁶ (1) García Vázquez et al., 1997 ⁷ (2) | | C |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|-------------------|-------------------------------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-----------------------|----------|
| Atosiban | Tractocile® 37.5 | Ferring | 24 h at 25 °C | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004 ⁶ | | D |
| Atosiban | Tractocile® 6.75 | Ferring | 24 h at 25 °C | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004 ⁶ | | D |
| Atracurium | Atracurio® 25 mg amp. | Inibsa | 1 month 30 °C (loss of 8%) | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004 ⁶ | | A |
| Basiliximab | Simulect® 20 mg vial | Novartis Farmaceutica | 4 days at <25 °C | Cuervas-Mons et al., 2004 ⁶ | | C |
| Bevacizumab | Avastin® 100 mg vial | Roche Farma | 9 h at 30 °C; 5 days at 15 °C | Consult lab 20/2/09 | 913248100 | D |
| | Avastin® 400 mg vial | Roche Farma | 9 h at 30 °C; 5 days at 15 °C | Consult lab 20/2/09 | 913248100 | D |
| BH4 | Tetrahydrobiopterin® 10 mg | Schircks Laboratories | ≤−20 °C: 36 months// ≤−10 °C: 18 months// ≤+5 °C: 4 months// >6 months at 25 °C: maintains >99.5% activity (although may turn yellow or break more easily)// 20–30 °C: expires in 2 months// Can be re-frozen | SmPCs (review year not available) | | A |
| BH4 | Tetrahydrobiopterin® 50 mg | Schircks Laboratories | ≤−20 °C: 36 months// ≤−10 °C: 18 months// ≤+5 °C: 4 months// >6 months at 25 °C: maintains >99.5% activity (although may turn yellow or break more easily)// 20–30 °C: expires in 2 months// Can be re-frozen | SmPCs (review year not available) | | A |

| | | | | | | |
|-------------|---------------------------------------|---------------------------------------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---|
| Bleomycin | Bleomicina® 15 IU vial | Almirall | 28 days | Cobos Campos et al., 2006, ³ Sala et al., 2004, ⁵ Cuervas-Mons et al., 2004, ⁶ Silgado et al., 2006 ² | | A |
| Busulphan | Busilvex® 60 mg vial | Pierre Fabre Iberica | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 20/02/09 | 934833000 | F |
| Calcitonin | Calcitonina Hubber® inject. 100 IU | Valeant Pharmaceuticals Iberica | 1 month | Cobos Campos et al., 2006 ³ | | A |
| Calcitonin | Calcitonina Hubber® nasal 200 IU | Valeant Pharmaceuticals Iberica | 1 month | Cobos Campos et al., 2006 ³ | | A |
| Carboprost | Hemabate® 250 | Zlb Behring | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 20/02/09 | 933068117 | F |
| Carmustine | BiCNU® (ME) 100 mg vial | Bms | The appearance of droplets indicates that the product is not fit to be used | Cobos Campos et al., 2006 ³ | | F |
| Caspofungin | Cancidas® 50 mg | Merck Sharp Dohme | 48 h | Cobos Campos et al., 2006, ³ Sala et al., 2004, ⁵ Cuervas-Mons et al., 2004, ⁶ Silgado et al., 2006 ² | | C |
| Caspofungin | Cancidas® 70 mg | Merck Sharp Dohme | 48 h | Cobos Campos et al., 2006, ³ Sala et al., 2004, ⁵ Cuervas-Mons et al., 2004, ⁶ Silgado et al., 2006 ² | | C |
| Cefonizid | Monocyd® 1 g IM/IV | Rottapharm | 18 months | Silgado et al., 2006, ² Cuervas-Mons et al., 2004 ⁶ | | A |
| Cetuximab | Erbitux® 100 mg vial | Merck Sharp Dohme | 20 h | Bovaira García et al., 2004 ⁴ | | D |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|----------------------------------|--------------------------|------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|-----------------------|-------------------------|
| Cisatracurium | Nimbex® 10 mcg/ml | Glaxo SmithKline | 1 month at 25 °C: 5% degradation 1 day outside fridge = 10 days in fridge | Cobos Campos et al., 2006, ³ Sala et al., 2004 ⁵ | | Specific recommendation |
| Cisatracurium | Nimbex® 2 mcg/ml | Glaxo SmithKline | 1 month at 25 °C: 5% degradation 1 day outside fridge = 10 days in fridge | Cobos Campos et al., 2006, ³ Sala et al., 2004 ⁵ | | Specific recommendation |
| Liposomal cytarabine | Depocyte® 50 mg vial | Mundi Pharma Pharmaceuticals | 72 h at 25 °C | Consult lab 20/02/09 | 913821870 | C |
| Chlorambucil | Leukeran® 2 mg tablets | Glaxo SmithKline | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 22/12/09 | 918070301 | F |
| Chloramphenicol | Colircusi cloranfenicol® | Alcon Cusi | Storage: 15 days at 25 °C Once open: 1 month | Bovaira García et al., 2004, ⁴ Silgado et al., 2006 ² | | B |
| Chloramphenicol | Colircusi de Icol® | Alcon Cusi | Storage: 15 days at 25 °C Once open: 1 month | Bovaira García et al., 2004 ⁴ | | B |
| Anti-inhibitor coagulant complex | Feiba® 4 1000 UF | Baxter | 6 months | Sala et al., 2004 ⁵ | | A |
| Daclizumab | Zenapax® 5 mg/ml | Roche Farma | 14 days at 25 °C, 7 days at 30 °C | Bovaira García et al., 2004, ⁴ Silgado et al., 2006 ² | | B |
| Daptomycin | Cubicin® 500 mg vial | Novartis Farmaceutica | 60 h at 25 °C | Consult lab 16/02/09 | 933064200 | C |
| Denileukin diftitox | Ontak® 300 mg/2 ml | Ferrer Farma | No information available | Consult lab 20/12/09 | 936003700 | F |
| Desmopressin | Minurin® drops | Ferring | 1 month | Cobos Campos et al., 2006, ³ Sala et al., 2004, ⁵ Cuervas-Mons et al., 2004 ⁶ | | A |

| | | | | | | |
|---------------------------------------|--------------------------------------------|----------------------|----------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---|
| Desmopressin | Minurin® inject | Ferring | 24 h | Cobos Campos et al., 2006, ³ Sala et al., 2004, ⁵ Cuervas-Mons et al., 2004 ⁶ | | D |
| Dinoprostone | Prepidil® 0.5 gel | Pfizer | 1 month | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004 ⁶ | | A |
| Dinoprostone | Propess® 10 mg | Ferring SAU | <24h at 2–8 °C: re-freeze. If thawed completely: 4 weeks at 2–8 °C. Room temperature: 24 h 1 month at 25 °C | Consult lab 03/08/09 | | D |
| Dinoprostone | Prostaglandina E2® 10 mg/ml | Pfizer | 1 month at 25 °C | Cobos Campos et al., 2006 ³ | | A |
| Dopamine hydrochloride | Duodopa gel intestinal cassettes 100 ml | Solvay Pharma | 4 days at 25 °C | Consult lab 05/03/09 | 934954500 | C |
| Dornase alpha | Pulmozyme® 2.5 mg amp. | Roche Farma | 24 h at 30 °C (1) 2.5 days at 30 °C (2) | Cuevas (1), Sala et al., 2004 ⁵ (1), Silgado et al., 2006 ² (2), Bovaira García et al., 2004 ⁴ (2) | | D |
| Doxycycline | Vibravenosa® 100 mg | Pfizer | 1 month | Cobos Campos et al., 2006 ³ | | A |
| Doxorubicin (=adriamycin) | Doxorrubicina® 50 mg vial | Ferrer Farma | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 20/02/09 | 936003700 | F |
| Liposomal doxorubicin | Myocet® 50 mg vial | Cephalon Pharma | <1 month | Cobos Campos et al., 2006, ³ Silgado et al., 2006 ² | | B |
| Pegylated liposomal doxorubicin | Caelyx® 20 mg vial | Schering-Plough | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab, Sala et al., 2004 ⁵ | | F |
| Drotrecogin | Xigris® 20 mg | Lilly | 72 h up to 28 °C | Silgado et al., 2006 ² | | C |
| Drotrecogin | Xigris® 5 mg | Lilly | 72 h up to 28 °C | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | C |
| Ecuzumab | Soliris® 300 mg vial | Alexion Pharma Spain | 6–7 days | Consult lab 20/02/09 | 932723017 | C |
| Epirubicin | Farmorubicina® 200 mg vial | Pfizer | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 15/02/09 | | F |

Table 2 (Continued)

| Eptifibatide Active Ingredient | Integrilin® 20 mg vial Drug Product | Glaxo SmithKline Manufacturing Laboratory | 2 months Stability at Room Temperature (22–25 °C) | Cuervas-Mons et al., 2004 ⁶ Reference | Contact Telephone No. | A Category |
|-------------------------------------|-------------------------------------|-------------------------------------------|------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|-------------------------|
| Erythropoietin alpha | Eprex® 40,000 IU prefilled syringe | Janssen-Cilag | 1 h 6 h | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004, ⁶ Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | | D |
| Erythropoietin beta | Neorecormon® prefilled syringe | Roche Farma | 3 days | Cuervas-Mons et al., 2004, ⁶ Cobos Campos et al., 2006, ³ Silgado, Sala et al., 2004 ⁵ | | C |
| Streptokinase | Streptase® 750,000 IU | CSL Behring | Keep at temperature ≤25 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | D |
| Streptozocin | Zanosar® (ME) 1 g vial | Pfizer | Note batch no., expiry, temperature and exposure time and contact laboratory | Cobos Campos et al., 2006, ³ Silgado et al., 2006 ² | | F |
| Etanercept | Enbrel® 25 mg prefilled syringe | Wyeth Farma | 24 h at ≤25 °C; >25 °C contact laboratory | Consult lab 21/12/09 | 913346400 | D |
| Etanercept | Enbrel® 25 ng/ml paediatric vial | Wyeth Farma | 24 h at ≤25 °C; >25 °C contact laboratory | Consult lab 21/12/09 | 913346400 | D |
| Etanercept | Enbrel® 50 mg prefilled syringe | Wyeth Farma | 24 h at ≤25 °C; >25 °C contact laboratory | Consult lab 21/12/09 | 913346400 | D |
| Factor IX | Factor® IX 600 IU | Behring | 3 months at 25 °C (do not re-refrigerate) | SmPCs (2010) | | Specific recommendation |
| Factor VIII + Von Willebrand factor | Fanhdi® | Grifols | 2 years at 25 °C (1) months at 40 °C (2) | Cobos Campos et al., 2006 ³ (1), Cuervas-Mons et al., 2004 ⁶ (2) | | A |
| Recombinant Factor VIII | Advate® 1000 IU | Baxter | 6 months at 25 °C (do not re-refrigerate) | SmPCs (review year not available) | | Specific recommendation |

| | | | | | | |
|-------------------------|-------------------------------|---------------------|-----------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|-----------|-------------------------|
| Recombinant Factor VIII | Advate® 500 IU | Baxter | 6 months at 25 °C (do not re-refrigerate) | SmPCs (review year not available) | | Specific recommendation |
| Factor IX plasma | Inmunine® Stim plus 600 | Baxter | 3 months at 25 °C | Sala et al., 2004 ⁵ | | A |
| Recombinant Factor IX | Benefix® 500 IU | Baxter | 1 month at 25 °C | Cuervas-Mons et al., 2004, ⁶ Silgado et al., 2006, ² Sala et al., 2004 ⁵ | | A |
| Recombinant Factor VIII | Refacto AF® 1000 IU vial 4 ml | Wyeth Farma | 3 months at 25 °C. After this time, do not re-refrigerate | SmPCs (review year not available) | | A |
| Recombinant Factor VIII | Refacto AF® 250 IU vial 4 ml | Wyeth Farma | 3 months at 25 °C. After this time, do not re-refrigerate | SmPCs (review year not available) | | A |
| Recombinant Factor VIII | Refacto AF® 500 IU vial 4 ml | Wyeth Farma | 3 months at 25 °C. After this time, do not re-refrigerate | SmPCs (review year not available) | | A |
| Factor VIIa | Novoseven® 1.2 | Novo Nordisk Pharma | 24 h at 25 °C | Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Sala et al., 2004, ⁵ Consult lab 18/02/09 | 913349800 | D |
| Factor VIIa | Novoseven® 2.4 | Novo Nordisk Pharma | 24 h at 25 °C | Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Sala et al., 2004, ⁵ Consult lab 18/02/09 | 913349800 | D |
| Factor VIIa | Novoseven® 4.8 | Novo Nordisk Pharma | 24 h at 25 °C | Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Sala et al., 2004, ⁵ Consult lab 18/02/09 | 913349800 | D |
| Phenylephrine | Colircusi fenilefrina® | Alcon Cusi | 1 month (1) 15 days (2) | SmPCs (1), Cobos Campos et al., 2006 ³ (2), Silgado et al., 2006 ² (2) | | B |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|-----------------------------|----------------------------|--------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------|
| Phentolamine | Regitine® | Novartis Farmaceutica | 7 days at 25 °C or 2 days at 30 °C | Consult lab 21/07/09 | 933064200 | B |
| Fibrin | Tissucol® 2 ml | Baxter | 48 h. Do not re-freeze | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | D |
| Filgrastim | Neupogen® 300 MU | Amgen | 7 days, 9–30 °C | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Silgado et al., 2006, ² Sala et al., 2004 ⁵ | | B |
| Filgrastim | Neupogen® 480 MU | Amgen | 7 days, 9–30 °C | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Silgado et al., 2006, ² Sala et al., 2004 ⁵ | | B |
| Filgrastim | Neupogen® vials | Amgen | 7 days, 9–30 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Silgado et al., 2006, ² Sala et al., 2004 ⁵ | | B |
| Fluorescein + oxybuprocaine | Colircusi fluotest® | Alcon Cusi | 15 days | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | | B |
| Folinic acid | Folinato calcico® 10 mg/ml | Ferrer Farma | 7–14 days at 25 °C | Consult lab 22/12/09 | 936003700 | B |
| Galsulfase | Naglazyme® 5 mg vial | Biomarin Europe Ltd | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 22/12/09 | 620988250 | F |
| Antiophidic immunoglobulin | Viperfav® | Sanofi Pasteur MSD | 7 days | Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | B |
| Anti D immunoglobulin 3 | Rhopylac® 300 mcg syr 2 ml | CSL Behring | 24 h at 25 °C | Consult lab 25/08/09 | 933671870 | D |

| | | | | | | |
|-----------------------------------|---------------------------------|--------------------|----------------------------------------------------------------------------------------------|----------------------------------------|-----------|-------------------------|
| Specific immunoglobulin | Gamma Anti D® 1500 IU | Grifols | 3 months at 25 °C, although discarding is recommended | Cobos Campos et al., 2006 ³ | | E |
| Specific immunoglobulin | Gamma Antihepatitis B 200 IU/ml | Grifols | 3 months at 25 °C, 2 months at 35 °C, although discarding is recommended | Cobos Campos et al., 2006 ³ | | E |
| Specific immunoglobulin | Gamma Antitetanos® 500 IU | Grifols | 12 months at 25 °C, 3 months at 35 °C, although discarding is recommended as it is a vaccine | Cobos Campos et al., 2006 ³ | | E |
| Specific immunoglobulin | Imogam® 150 IU/ml | Sanofi Pasteur MSD | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 21/12/09 | 913717800 | F |
| Non specific human immunoglobulin | Kiovig® 10 g | Baxter | 9 months (do not re-refrigerate) | SmPCs (2006) | | Specific recommendation |
| Non specific human immunoglobulin | Kiovig® 2.5 g | Baxter | 9 months (do not re-refrigerate) | SmPCs (2006) | | Specific recommendation |
| Non specific human immunoglobulin | Kiovig® 5 g | Baxter | 9 months (do not re-refrigerate) | SmPCs (2006) | | Specific recommendation |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|-----------------------------------|---------------------------------------------|--------------------------|------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|-------------------------|
| Non specific human immunoglobulin | Vivaglobin® 160 | CSL Behring | 3 months or until expiry date if earlier (do not re-refrigerate) | SmPCs (2008) | | Specific recommendation |
| Gemtuzumab | Mylotarg® 5 mg vial | Wyeth Farma | 90 days | Sala et al., 2004 ⁵ | | A |
| Glatiramer | Copaxone® 20 mg prefilled syringe | Sanofi-Aventis | 7 days, 15–25 °C | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Silgado et al., 2006, ² Sala et al., 2004 ⁵ | | B |
| Gonadotrophin | Gonal F® 300 IU 22 mcg/0.5 ml pref. pen | Serono Spain | 3 months | Consult lab 21/12/09 | 917454400 (Merck) | A |
| Gonadotrophin | Gonal F® 450 IU 33 mcg/0.75 ml pref. pen | Serono Spain | 3 months | Consult lab 21/12/09 | 917454400 (Merck) | A |
| Gonadotrophin | Ovitrelle® 250 mcg prefilled syringe | Serono Spain | 30 days | Consult lab 21/12/09 | 917454400 | A |
| Gonadotrophin | Puregon® 300 IU cassette 0.36 ml | Organon Spain | 3 months at <25 °C, once open 1 month | Consult lab 05/03/09 | 915673000 | A |
| Gonadotrophin | Puregon® 600 IU cassette 0.72 ml | Organon Spain | 3 months at <25 °C, once open 1 month | Consult lab 05/03/09 | 915673000 | A |
| Gonadotrophin | Puregon® 900 IU cassette 1.08 ml | Organon Spain | 3 months at <25 °C, once open 1 month | Consult lab 05/03/09 | 915673000 | A |
| Hyaluronate | Healon® ‘‘5’’ 23 mg/ml prefilled syringe | Panalab | 30 days 25 °C | Cobos Campos et al., 2006 ³ | | A |
| Hemin | Normosang® 250 mg vial | Orphan Europe | 1 week up to 26 °C | Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | B |
| Infliximab | Remicade® 100 vial | Schering Plough | 12 months | Cobos Campos et al., 2006 ³ | | A |
| C1 esterase inhibitor | Beriner® 500 IU vial | Csl Behring | Stable, can be stored at temps up to 25 °C | SmPCs (review year not available) | | A |

| | | | | | | |
|--------------------------|-----------------------------------------|---------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|-----------|-------------------------|
| Insulin | Insuman infusat® 100 U | Sanofi-Aventis | Storage: no information available Once in use: 4 weeks | Consult lab 21/12/09 | 934859400 | Specific recommendation |
| Insulin glargine | Lantus® 100 U/ml solostar | Sanofi-Aventis | 4 weeks at <30 °C (including usage time) | Bovaira García et al., 2004 ⁴ | | A |
| Insulin aspart | Novorapid flexpen® 100 U/ml pens | Novo Nordisk Pharma | Storage: 24 h at 25 °C. Once in use: 4 weeks | Bovaira García et al., 2004 ⁴ | | D |
| Insulin aspart-protamine | Novomix 30 flexpen® 100 U/ml pref. pens | Novo Nordisk Pharma | Storage: 24 h at 25 °C. Once in use: 4 weeks | Bovaira García et al., 2004 ⁴ | | D |
| Insulin detemir | Levemir® 100 U/ml | Novo Nordisk Pharma | Once in use: 6 weeks (do not re-refrigerate once open or if carried as a spare) | SmPCs (review year not available) | | Specific recommendation |
| Insulin glulisine | Apidra® 100 U/ml solostar | Sanofi-Aventis | 4 weeks (including administration time) | SmPCs (review year not available) | | Specific recommendation |
| Insulin regular | Actrapid® 100 IU/ml vial | Novo Nordisk Pharma | Storage: 24 h at 9–25 °C Once in use: 6 weeks | Cobos Campos et al., 2006, ³ Consult lab 25/08/09 | 913349800 | D |
| Insulin regular | Actrapid innolet® 100 IU/ml pref. pen | Novo Nordisk Pharma | Storage: 24 h at 9–25 °C Once in use: 4 weeks | Cobos Campos et al., 2006, ³ Consult lab 25/08/09 | 913349800 | D |
| Insulin protamine | Insulatard® 100 IU/ml vial | Novo Nordisk Pharma | Storage: 24 h at 9–25 °C. Once in use: 4 weeks | Cobos Campos et al., 2006 ³ | | D |
| Insulin protamine | Insulatard flexpen® 100 IU/ml pref. pen | Novo Nordisk Pharma | | | | D |
| Insulin protamine | Insulatard innolet® 100 IU/ml | Novo Nordisk Pharma | | | | D |
| Insulin regular-isophane | Humulina® 20:80 pen 100 U/ml | Lilly | Storage: 4 days (20 °C), 48 h (25 °C), 24 h (30 °C), 12 h (35 °C). Once in use: 28 days (25 °C) | Bovaira García et al., 2004 ⁴ | | C |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|---------------------------|----------------------------------------|--------------------------|-------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------|
| Insulin regular-isophane | Humulina® 30:70 pen 100 U/ml | Lilly | Storage: 4 days (20 °C), 48 h (25 °C), 24 h (30 °C), 12 h (35 °C). Once in use: 28 days (25 °C) | Bovaira García et al., 2004 ⁴ | | C |
| Insulin regular-protamine | Mixtard 20 innolet® 100 IU/ml | Novo Nordisk Pharma | Storage: 24 h at 9–25 °C. Once in use: 4 weeks | Cobos Campos et al., 2006 ³ | | D |
| Insulin regular-protamine | Mixtard 30 innolet® 100 IU/ml | Novo Nordisk Pharma | Storage: 24 h at 9–25 °C. Once in use: 4 weeks | Cobos Campos et al., 2006 ³ | | D |
| Insulin lispro | Humalog® 100 IU/ml vial | Lilly | Storage: 7 days (20 °C), 48 h (25 °C), 24 h (30 °C), 12 h (35 °C). Once in use: 28 days (25 °C) | Cobos Campos et al., 2006, ³ SmPCs (review year not available) | | C |
| Insulin lispro | Humalog humaject® 100 U/ml pref. pen | Lilly | Storage: 7 days (20 °C), 48 h (25 °C), 24 h (30 °C), 12 h (35 °C). Once in use: 28 days (25 °C) | Cobos Campos et al., 2006, ³ SmPCs (review year not available) | | C |
| Insulin lispro | Humalog pen® 100 U/ml pref. pen | Lilly | Storage: 7 days (20 °C), 48 h (25 °C), 24 h (30 °C), 12 h (35 °C). Once in use: 28 days (25 °C) | Cobos Campos et al., 2006, ³ SmPCs (review year not available) | | C |
| Insulin lispro-protamine | Humalog MIX25 pen® 100 IU/ml pref. pen | Lilly | Storage: 7 days (20 °C), 48 h (25 °C), 24 h (30 °C), 12 h (35 °C). Once in use: 28 days (25 °C) | Cobos Campos et al., 2006, ³ SmPCs (review year not available) | | C |
| Insulin zinc | Monotard® 100 IU/ml vial | Novo Nordisk Pharma | Storage: 24 h at 25 °C. Once in use: 6 weeks | Cobos Campos et al., 2006 ³ | | D |
| Interferon 2A | Intron A® 10 MIU vial solution | Schering-Plough | 7 days | Cobos Campos et al., 2006, ³ Bovaira García et al., 2004, ⁴ Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | B |

| | | | | | | |
|-----------------------|---------------------------------|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-------------------------|
| Interferon 2A | Intron A® 18MIU pen | Schering-Plough | 48 h at 25 °C | Bovaira García et al., 2004, ⁴ Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | C |
| Interferon 2A | Intron A® 60MIU pen | Schering-Plough | 48 h at 25 °C | Bovaira García et al., 2004, ⁴ Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | C |
| Interferon B-1A | Rebif® 22 mcg prefilled syringe | Serono Spain | Storage: 6 days 25 °C. Once in use: 1 month | Silgado et al., 2006, ² Cobos Campos et al., 2006, ³ Bovaira García et al., 2004, ⁴ Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | C |
| Interferon B-1A | Rebif® 44 mcg prefilled syringe | Serono Spain | Storage: 6 days 25 °C. Once in use: 1 month | Silgado et al., 2006, ² Cobos Campos et al., 2006, ³ Bovaira García et al., 2004, ⁴ Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | C |
| Isoprenaline | Aleudrina® 0.2 mg vial | Reig Jofre | 6 months at 25 °C (at this temperature, reduce expiry 3 months) | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Lactobacilli | Casentilus® | Casen Fleet | 24 h | Silgado et al., 2006 ² | | D |
| Laronidase | Aldurazyme® 500 IU vial | Genzyme | 6 months at 25 °C | Consult lab 26/02/09 | 916591670 | A |
| Latanoprost | Xalatan® eye drops | Pfizer | 1 month at 25 °C | SmPCs, Bovaira García et al., 2004 ⁴ | | A |
| Latanoprost + timolol | Xalocom® eye drops | Pfizer | 1 month at 25 °C | SmPCs, Bovaira García et al., 2004 ⁴ | | A |
| Leuprolide | Eligard® | Astellas Pharma | 14 days at room temperature before use | Consult lab 21/12/09 | 914952700 | B |
| Levosimendan | Simdax® 2.5 mg/ml | Orion Corporation | Storage time (contact laboratory if exceeded): >25 °C: not acceptable 15–25 °C: 2–3 days 8–15 °C: 1 week 0–2 °C: 1 week <0 °C: 1 week | Consult lab 21/12/09 | 915030252 | F |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|-----------------------------------------------------|-------------------------------------------|--------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------|-----------------------|-------------------------|
| LHRH | LHRH® | Ferring | 15 days at 25 °C | Consult lab 16/02/09 | 917994780 | B |
| Organ preservation fluid | Viaspan® | Bristol Myers | Use not recommended 12–24 h after breaking chain | Consult lab 18/02/09 | 914565300 | D |
| Lopinavir + ritonavir | Kaletra® oral solution 60ml | Abbott Laboratories | 42 days | SmPCs, Silgado et al., 2006, ² Cobos Campos et al., 2006 ³ | | A |
| Tetryzoline + medroxyprogesterone + chloramphenicol | Colircusi medrivás® | Alcon Cusi | Storage: 15 days 25 °C. Once in use: 1 month | Consult lab 20/2/09, Bovaira García et al., 2004 ⁴ | 934977000 | B |
| Melphalan | Melfalan® 2 mg tablets | Lilly | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 21/12/09 | 916635000 | F |
| Methylergometrine | Methergin® 0.2 mg/ml | Novartis Farmaceutica | 2 weeks | Cobos Campos et al., 2006, ³ Silgado et al., 2006 ² | | B |
| Methoxy peg epoetin beta | Mircera® 100 mcg/0.3 ml prefilled syringe | Roche Farma | 1 month at ≤30 °C. Do not re-refrigerate | Consult lab 21/12/09 | 913248100 | Specific recommendation |
| Methoxy peg epoetin beta | Mircera® 150 mcg/0.3 ml prefilled syringe | Roche Farma | 1 month at ≤30 °C. Do not re-refrigerate | Consult lab 21/12/09 | 913248100 | Specific recommendation |
| Methoxy peg epoetin beta | Mircera® 200 mcg/0.3 ml prefilled syringe | Roche Farma | 1 month at ≤30 °C. Do not re-refrigerate | Consult lab 21/12/09 | 913248100 | Specific recommendation |
| Methoxy peg epoetin beta | Mircera® 250 mcg/0.3 ml prefilled syringe | Roche Farma | 1 month at ≤30 °C. Do not re-refrigerate | Consult lab 21/12/09 | 913248100 | Specific recommendation |
| Methoxy peg epoetin beta | Mircera® 50 mcg/0.3 ml prefilled syringe | Roche Farma | 1 month at ≤30 °C. Do not re-refrigerate | Consult lab 21/12/09 | 913248100 | Specific recommendation |
| Methoxy peg epoetin beta | Mircera® 75 mcg/0.3 ml prefilled syringe | Roche Farma | 1 month at ≤30 °C. Do not re-refrigerate | Consult lab 21/12/09 | 913248100 | Specific recommendation |

| | | | | | | |
|--------------|----------------------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---|
| Muromonab | Orthodone® OKT3 | CILAG Gmbh | 1 week at 30 °C if at least 6 months of expiry period is left. 48 h at 25 °C if 3 months of expiry period is left | Cuervas-Mons et al., 2004 ⁶ | | C |
| Natalizumab | Tysabri® 300 mg 1 vial perfusion | Elan Farma | No information available | Consult lab 06/03/09 | 935677880 | F |
| Nonacog alfa | Benefix® 500 IU/1000 IU | Baxter | 1 month at ≤25 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | A |
| Octreotide | Sandostatin® 0.05 mg/ml | Novartis Farmaceutica | 14 days at <30 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | B |
| Octreotide | Sandostatin® 0.1 mg/ml | Novartis Farmaceutica | 14 days at <30 °C | Silgado et al., 2006, ² Cuervas-Mons et al., 2004 ⁶ | | B |
| Omalizumab | Xolair® 150 mg vial | Novartis Farmaceutica | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 18/02/09 | 933064200 | F |
| Oxytocin | Syntocinón® 10 IU/ml | Defiante Farmaceutica Lda | 3 months at <30 °C | Cobos Campos et al., 2006 ³ | | A |
| Oxytocin | Syntocinon® 10 IU/ml | Defiante Farmaceutica Lda | 3 months at <30 °C | Cobos Campos et al., 2006 ³ | | A |
| Palivizumab | Synagis® 100 | Abbott Laboratories | 2 weeks at <25 °C | Silgado et al., 2006, ² Sala et al., 2004 ⁵ | | B |
| Palivizumab | Synagis® 50 | Abbott Laboratories | 2 weeks | Sala et al., 2004 ⁵ | | B |
| Panitumumab | Vectibix® 100 mg vial | Amgen | 24 h at 25 °C | Consult lab 20/2/09 | 936001900 | D |
| Panitumumab | Vectibix® 400 mg vial | Amgen | 24 h at 25 °C | Consult lab 16/02/09 | 936001900 | D |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|------------------------|------------------------------------|--------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------|
| Pegaptanib sodium | Macugen® 0.3 prefilled syringe | Pfizer | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 04/03/09 | 932213366 | F |
| Pegfilgrastim | Neulasta® 6 mg prefilled syringe | Amgen | 72 h at <30 °C | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | C |
| Peginterferon alpha 2a | Pegasys® 135 mcg prefilled syringe | Roche Farma | 7 days | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | B |
| Peginterferon alpha 2a | Pegasys® 180 mcg prefilled syringe | Roche Farma | 7 days | Cuervas-Mons et al., 2004, ⁶ Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | | B |
| Peginterferon alpha 2b | Pegintron® 100 mcg pref. pen | Schering-Plough | 18 months at <25 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | A |
| Peginterferon alpha 2b | Pegintron® 120 mcg pref. pen | Schering-Plough | 18 months at <25 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | A |
| Peginterferon alpha 2b | Pegintron® 150 mcg pref. pen | Schering-Plough | 18 months at <5 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | A |
| Peginterferon alpha 2b | Pegintron® 50 mcg pref. pen | Schering-Plough | 18 months at <5 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | A |
| Peginterferon alpha 2b | Pegintron® 80 mcg pref. pen | Schering-Plough | 18 months at <25 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | A |

| | | | | | | |
|-------------|-------------------------------------|--------------------------|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---|
| Protamine | Protamina® Rovi 50 mg vial | Rovi | 48 h at 25 °C – 1 week | Cobos Campos et al., 2006, ³ Sala et al., 2004 ⁵ | | C |
| Prothrombin | Prothromplex Inmuno® Tim4 600 IU | Baxter | 6 months | Sala et al., 2004 ⁵ | | A |
| Ranibizumab | Lucentis® 10 mg vial | Novartis Farmaceutica | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 16/02/09 | 933064200 | F |
| Rasburicase | Fasturtec® 1.5 mg vial | Sanofi-Aventis | 15 days at 25 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | B |
| Risperidone | Risperdal® 25 mg | Janssen-Cilag | 7 days | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | B |
| Risperidone | Risperdal® 37.5 mg | Janssen-Cilag | 7 days | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | B |
| Risperidone | Risperdal® 50 mg | Janssen-Cilag | 7 days | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004 ⁵ | | B |
| Ritonavir | Norvir® 100 mg soft capsules | Abbott Laboratories | 1 month at <25 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004, ⁵ Bovaira García et al., 2004 ⁴ | | A |
| Rituximab | Mabthera® 100 mg vial | Roche Farma | 18 days at <30 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | B |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|-----------------------|--------------------------------------|--------------------------|----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|-------------------------|
| Rituximab | Mabthera® 500 mg vial | Roche Farma | 18 days at <30 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | B |
| Rocuronium | Esmeron® 100 mg vial | Organon Spain | 12 weeks at <30 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004, ⁵ Bovaira García et al., 2004 ⁴ | | A |
| Rotigotine | Neupro® patches | Ucb Pharma | 7 days at 25 °C | Consult lab 25/08/09 | 915703444 | B |
| Measles-Mumps-Rubella | Vacuna® MSD triple | Sanofi Pasteur MSD | 7 days at 25 °C | Cobos Campos et al., 2006 ³ | | B |
| Secretin | Secrelux® | Sanochemia | 3 weeks at 25 °C | Bovaira García et al., 2004, ⁴ García Vázquez et al., 1997 ⁷ | | B |
| Sirolimus | Rapamune® 1 mg tablets | Wyeth Farma | 24 h at 25 °C | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Sala et al., 2004, ⁵ Bovaira García et al., 2004 ⁴ | | D |
| Somatrophin | Zomacton® 4 mg | Ferring | 24–48 h | Consult lab 16/02/09 | 917994780 | D |
| Somatrophin | Genotonorm kabipen® 12 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 0.2 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 0.4 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |

| | | | | | | |
|-------------|--------------------------------------|---------------------|----------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------|-------------------------|
| Somatrophin | Genotonorm miniquick® 0.6 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 0.8 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 1 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 1.2 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 1.4 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 1.6 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 1.8 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Genotonorm miniquick® 2 mg vial | Pfizer | 6 months at 25 °C (including use). Do not re-refrigerate | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | Specific recommendation |
| Somatrophin | Humatrope® 12 mg cassette | Lilly | 6 days at 8–25 °C, 72 h at 25–30 °C, 24 h at 30–40 °C | Bovaira García et al., 2004 ⁴ | | C |
| Somatrophin | Humatrope® 24 mg cassette | Lilly | 6 days at 8–25 °C, 72 h at 25–30 °C, 24 h at 30–40 °C | Bovaira García et al., 2004 ⁴ | | C |
| Somatrophin | Humatrope® 6 mg cassette | Lilly | 6 days at 8–25 °C, 72 h at 25–30 °C, 24 h at 30–40 °C | Bovaira García et al., 2004 ⁴ | | C |
| Somatrophin | Norditropin® simplexx 10 mg | Novo Nordisk Pharma | 24 h at <25 °C | Consult lab 05/03/09, Bovaira García et al., 2004 ⁴ | 913349800 | D |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|----------------------|-------------------------------------|--------------------------|----------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------|
| Somatrophin | Norditropin® simplexx 15 mg | Novo Nordisk Pharma | 24 h at <25 °C | Consult lab 05/03/09, Bovaira García et al., 2004 ⁴ | 913349800 | D |
| Somatrophin | Norditropin® simplexx 5 mg | Novo Nordisk Pharma | 24 h at <25 °C | Consult lab 05/03/09, Bovaira García et al., 2004 ⁴ | 913349800 | D |
| Somatrophin | Nutropin® AQ 10 mg (30 IU) cassette | Ipsen Farma | Discard (no information available) | Consult lab 21/12/09 | 936858100 | E |
| Somatrophin | Omnitrope® 3.3 mg/ml vial | Sandoz Farmaceutica | 1 day at 25 °C and 15 days at 15 °C, 2 weeks at 0 °C or between –2 °C and –5 °C | Consult lab 23/3/09 | 917401280 | D |
| Pulmonary surfactant | Curosurf® 120 | Chiesi Spain | 24 h at <25 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Consult lab 17/02/09 | 934948000 | D |
| Pulmonary surfactant | Curosurf® 240 | Chiesi Spain | 24 h at <25 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Consult lab 17/02/09 | 934948000 | D |
| Suxamethonium | Anectine® 100 mg vial | Glaxo SmithKline | 2 weeks at 25 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Cuervas-Mons et al., 2004, ⁶ García et al., 2004 ⁴ | | B |
| Temsirolimus | Torisel® 25 mg vial | Wyeth Farma | 24 h at 25 °C; note batch no., expiry, temperature, exposure time and contact laboratory. (cadena_de.frio@wyeth.com) | Consult lab 20/2/09 | 913346400 | F |
| Tetracosactide | Nuvacthen Depot® | Defiante Farmaceutica | 1–3 months at <25 °C | García Vázquez et al., 1997, ⁷ Sala et al., 2004 ⁵ | | A |

| | | | | | | |
|------------------------|-------------------------------|----------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---|
| Tetracosactide | Synacthen® | Novartis Farmaceutica | 3–4 h at <25 °C | Silgado et al., 2006, ² Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004 ⁶ | | D |
| Thymoglobulin | Timoglobulina® 25 mg vial | Genzyme | 24 h at <37 °C | Silgado et al., 2006 ² | | D |
| Thiotepa | Tioplex® 15 mg vial | Addiene | 3 months at 25 °C (Oncothiotepa) | Silgado et al., 2006 ² | | A |
| Tipranavir | Aptivus® 250 mg soft capsules | Boehringer Ingelheim Spain | Storage: 60 days, 15–30 °C. Once in use: 60 days at <25 °C | Consult lab 21/12/09 | 934045100 | A |
| Thyrotropin alpha | Thyrogen® 0.9 mg vial | Genzyme | 1–2 years | Cuervas-Mons et al., 2004, ⁶ Cobos Campos et al., 2006, ³ Sala et al., 2004, ⁵ Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | | A |
| Tobramycin | Tobi® 300 mg 56 amp. 5 ml | Chiron Iberia | 1 month at 25 °C | Cuervas-Mons et al., 2004, ⁶ Silgado et al., 2006, ² Bovaira García et al., 2004, ⁴ Sala et al., 2004 ⁵ | | A |
| Topotecan | Hycamtin® 0.25 mg capsules | Glaxo SmithKline | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 20/02/09 | 918070301 | F |
| Topotecan | Hycamtin® 1 mg capsules | Glaxo SmithKline | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 20/02/09 | 918070301 | F |
| Toxin A, Cl. botulinum | Dysport® 500 IU vial | Ipsen Pharma | 3 days | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Arrixaca, Sala et al., 2004 ⁵ | | C |
| Botulinum toxin | Botox® 100 U | Allergan Sau | 14 days at 25 °C; 7 days at 30 °C | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | B |
| Botulinum toxin | Botulismus-antitoxin Behring® | Esteve | 1 week at 37 °C | Bovaira García et al., 2004 ⁴ | | B |
| Trabectedin | Yondelis® 0.25 mg vial | Pharmamar | 72 h at 25 °C | Consult lab 25/10/07 | 918466000 | C |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|-----------------------------------------|----------------------------------|--------------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------|
| Trabectedin | Yondelis® 1 mg vial | Pharmamar | 72 h at 25 °C | Consult lab 25/10/07 | 918466000 | C |
| Trastuzumab | Herceptin® 150 mg vial | Roche Farma | 30 days at 40 °C, 3 days at 50 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Arrixaca | | A |
| Trientine hydrochloride | Syprine® | Merck Sharp Dohme | 7 days | García Vázquez et al., 1997 ⁷ | | B |
| Tuberculin | Tuberculina® PPD | Ucb Pharma | 6 months at 25 °C, 2 weeks at 35 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006 ² | | A |
| Meningococcal C vaccine | Meningitec® prefilled syringe | Wyeth Farma | 24 h at <25 °C | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | | D |
| Diphtheria, tetanus, pertussis vaccine | Boostrix® 0.5 ml syringe | Glaxo SmithKline | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 25/08/09 | 918070467 | F |
| DTP and hepatitis B vaccine | Tritanrix® | Glaxo SmithKline | 2 weeks at 21 °C; 1 week at 37 °C. Although, as it is a vaccine, it is recommended to be discarded | Bovaira García et al., 2004 ⁴ | | E |
| DtaP vaccine | Infanrix® | Glaxo SmithKline | 2 weeks at 21 °C; 1 week at 37 °C. Although, as it is a vaccine, it is recommended to be discarded | Cobos Campos et al., 2006, ³ Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | | E |
| <i>Haemophilus influenzae</i> b vaccine | Hiberix® | Glaxo SmithKline | 2 weeks at 21 °C; 1 week at 37 °C. Although, as it is a vaccine, it is recommended to be discarded | Silgado et al., 2006 ² , Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | E |
| Hepatitis B vaccine | Twinrix® adult prefilled syringe | Glaxo SmithKline | Note batch no., expiry, temperature, exposure time and contact laboratory | Consult lab 25/08/09 | 918070467 | F |
| Pneumococcal conjugate vaccine | Prevenar® prefilled syringe | Wyeth Farma | 24 h at ≤25 °C. Although, as it is a vaccine, it is recommended to be discarded | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | E |

| | | | | | | |
|--------------------------------|-------------------------|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|-----------|---|
| Rabies vaccine | Rabipur® | Novartis Farmaceutica | 1 year at 25 °C; 3 months at >37 °C; 1 month at >55 °C. Although, as it is a vaccine, it is recommended to be discarded | Consult lab 01/04/06 | 933064200 | E |
| Varicella vaccine | Varilrix® | Glaxo SmithKline | 1 week at 21 °C. Although, as it is a vaccine, it is recommended to be discarded | Bovaria García et al., 2004, ⁴ Silgado et al., 2006 ² | | E |
| Hepatitis A vaccine | Havrix® 1440 | Glaxo SmithKline | 2 weeks at 21 °C; 1 week at 37 °C. Although, as it is a vaccine, it is recommended to be discarded | Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | E |
| Hepatitis A vaccine | Havrix® 720 | Glaxo SmithKline | 2 weeks at 21 °C; 1 week at 37 °C. Although, as it is a vaccine, it is recommended to be discarded | Silgado et al., 2006, ² Cuervas-Mons et al., 2004, ⁶ Bovaira García et al., 2004 ⁴ | | E |
| Meningococcal C vaccine | Menjugate® | Esteve | 6 months at 30 °C, 1 week at 40 °C (without reducing expiry period). Although, as it is a vaccine, it is recommended to be discarded | Cobos Campos et al., 2006, ³ Bovaira García et al., 2004 ⁴ | | A |
| Hepatitis B vaccine | Engerix-B® 10 mcg | Glaxo SmithKline | 2 weeks 21 °C, 1 week 37 °C | Cobos Campos et al., 2006 ³ | | B |
| Hepatitis B vaccine | Engerix-B® 20 mcg | Glaxo SmithKline | 3 weeks 21 °C, 1 week 37 °C | Cobos Campos et al., 2006 ³ | | B |
| Tetanus and diphtheria vaccine | Diftavax® 40/4 IU adult | Sanofi Pasteur Msd | 14 days at 25 °C | Silgado et al., 2006 ² | | B |

Table 2 (Continued)

| Active Ingredient | Drug Product | Manufacturing Laboratory | Stability at Room Temperature (22–25 °C) | Reference | Contact Telephone No. | Category |
|--------------------------------|---------------------------------|--------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|-----------------------|----------|
| Tetanus and diphtheria vaccine | Ditanrix® 20/2 IU adult | Glaxo Smithk | 2 weeks at 21 °C, 1 week at 37 °C | Cobos Campos et al., 2006 ³ | | B |
| Inactivated polio vaccine | Vacuna Poliometitica Berna® | Berna Biotech Spain | Temperature ≤25 °C: <24 h: reduce expiry period by 2 months >24 h and <72 h: reduce expiry period by 4 months >72 h and <120 h: reduce expiry period by 6 months >120 h: discard | Cobos Campos et al., 2006 ³ | | D |
| Vinblastine | Vinblastina® 10 mg vial | Stada | 21 days at 15 °C and 14 days at 25 °C | Consult lab 20/2/09 | 934738889 | B |
| Vincristine | Vincristina® 2 mg vial | Pfizer | 24 h at 25 °C | Cobos Campos et al., 2006, ³ Cuervas-Mons et al., 2004 ⁶ | | D |
| Vinorelbine | Navelbine® 20 mg capsules | Pierre Fabre Iberica | 1 month at <25 °C, 15 days at <30 °C, can be frozen | Consult lab 20/2/09, Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | 934833000 | A |
| Vinorelbine | Navelbine® 30 mg capsules | Pierre Fabre Iberica | 1 month at <25 °C, 15 days at <30 °C, can be frozen | Consult lab 20/2/09, Silgado et al., 2006, ² Bovaira García et al., 2004 ⁴ | 934833000 | A |
| Vinorelbine | Navelbine® 50 mg vial | Pierre Fabre Iberica | 1 month at <25 °C, 15 days at <30 °C, <48 h at >30 °C or exposed to the light. Can be frozen | Consult lab 21/12/09 | 914909900 | A |
| Voriconazole | Vfend® 40 mg/ml oral suspension | Pfizer | 30 days at 25 °C (temperature excursions are cumulative, so contact the laboratory for an individual evaluation) | Consult lab 21/12/09 | 914909900 | A |
| Hyaluronic acid viscoelastic | Provisc® | Alcon Cusi | 12 h at 25 °C | Consult lab 26/08/09 | 934977000 | D |


|  Govern de les Illes Balears Hospital Universitari Son Dureta Pharmacy department | BREAK IN THE COLD CHAIN STANDARD OPERATING PROCEDURE | Date issued 01/01/10 | | | | | | | | | | | | | | | | | | | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|-------------------------|----------|----------------|--------|---|------------------------------------|-------|---|----------------------------------|-------|---|----------------------|-------|---|----------------------|-----------------------|---|--------------------------------------|---------|---|--------------------------------|--------------------|
| | | Valid until 01/01/11 | | | | | | | | | | | | | | | | | | | | | |
| <p>All refrigerators must have a temperature sensor or a temperature control probe.</p> <p>The refrigerator temperatures must be checked at 8am every day by a pharmacy assistant.</p> <p>If temperature is >8°C, inform the pharmacist who will download the temperature monitoring and assess the incident.</p> <p>If the temperature has been between 8-12°C for a period <8 hours, no action must be taken.</p> <p>If the period is >8 hours or the refrigerator temperature has exceeded 12°C, the following steps must be taken:</p> <ol style="list-style-type: none"> 1. Record the incident, indicating the temperature reached and time. 2. Make a list of the drugs, the quantity and withdraw the affected packages. 3. Review of stability of each of them. 4. Label all category A, B and C medications affected as follows: <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p style="text-align: center;">Safety Notice</p> <p style="text-align: center;">This medicine was outside of the refrigerator for ... (hours) on.... (day).</p> <p style="text-align: center;">It can still be used</p> </div> 5. Evaluate category D drugs according to specific information and type of medication. 6. Dispose of category E medications. Vaccines are always disposed of, whatever their stability. 7. Contact the laboratory if a batch-dependent drug is affected. <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Category</th> <th>Stability >8°C</th> <th>Action</th> </tr> </thead> <tbody> <tr> <td>A</td> <td>Stable ≥ 1 month (28 days) at 25°C</td> <td>Label</td> </tr> <tr> <td>B</td> <td>Stable ≥ 1 week (7 days) at 25°C</td> <td>Label</td> </tr> <tr> <td>C</td> <td>Stable ≥ 48h at 25°C</td> <td>Label</td> </tr> <tr> <td>D</td> <td>Stable < 48h at 25°C</td> <td>Evaluate individually</td> </tr> <tr> <td>E</td> <td>Not stable outside the fridge (>8°C)</td> <td>Discard</td> </tr> <tr> <td>F</td> <td>Stability depends on the batch</td> <td>Consult laboratory</td> </tr> </tbody> </table> | | | Category | Stability >8°C | Action | A | Stable ≥ 1 month (28 days) at 25°C | Label | B | Stable ≥ 1 week (7 days) at 25°C | Label | C | Stable ≥ 48h at 25°C | Label | D | Stable < 48h at 25°C | Evaluate individually | E | Not stable outside the fridge (>8°C) | Discard | F | Stability depends on the batch | Consult laboratory |
| Category | Stability >8°C | Action | | | | | | | | | | | | | | | | | | | | | |
| A | Stable ≥ 1 month (28 days) at 25°C | Label | | | | | | | | | | | | | | | | | | | | | |
| B | Stable ≥ 1 week (7 days) at 25°C | Label | | | | | | | | | | | | | | | | | | | | | |
| C | Stable ≥ 48h at 25°C | Label | | | | | | | | | | | | | | | | | | | | | |
| D | Stable < 48h at 25°C | Evaluate individually | | | | | | | | | | | | | | | | | | | | | |
| E | Not stable outside the fridge (>8°C) | Discard | | | | | | | | | | | | | | | | | | | | | |
| F | Stability depends on the batch | Consult laboratory | | | | | | | | | | | | | | | | | | | | | |
| <p>8. Breaks in the cold chain have a cumulative effect on the drug. If a drug has been affected by a previous cold chain break, consult the manufacturing laboratory.</p> | | | | | | | | | | | | | | | | | | | | | | | |

Figure 1 Standard operating procedure for a break in the cold chain.

Finally, agreement was reached within the pharmacy department on a standard operating procedure (SOP) for any break in the cold chain, which sorted the drugs into 6 categories based on the time they were stable outside of the refrigerator (Table 1).

Results

A total of 254 medicinal products corresponding to 162 active ingredients were reviewed (Table 2).

The number of drugs in each classification was as follows: (A) 65, (B) 47, (C) 30, (D) 47, (E) 12, and (F) 22. There were also specific recommendations for each category, as follows, provided that the time and temperature limits stipulated for each category were not exceeded:

- A, B, and C: Establish a control and monitoring system by labelling (Fig. 1).
- D: Continue in use if it was a one-off break in the cold chain and did not exceed the established maximum time. Otherwise, dispose of or return the drug to the laboratory.
- E: Dispose of or return the drug to the laboratory.

There were 31 drugs that could not be included in any category, so it is recommended to check the specific information regarding room temperature stability in Table 2.

The information obtained is available on the hospital intranet, in the "manuales de procedimiento" section of the pharmacotherapy portal. There is also a version on the Internet, in the free access pharmacy department portal (see URL at the end of the article).¹¹

Discussion and Conclusions

The methodology used to conduct this review was similar to that used in the aforementioned studies.²⁻¹⁰ However, there are differences in the information given by certain pharmaceutical laboratories. This may be because the drug companies involved have carried out further stability studies during the time between the completions of both reviews.

One problem found was the differences in stability data for the same active ingredient, depending on the laboratory that undertook the study. We agree with Cobos Campos et al.³ who suggested that laboratories should conduct their stability studies under the same temperature conditions to standardise them and facilitate comparison. However, it is important to consult the information available at each centre for the drug product in question.

It was deemed necessary to have stability data for all drugs to be incorporated in the hospital guide upon inclusion, and for the laboratory to provide degradation tables, as a query made when the chain is broken is urgent, and the laboratory cannot guarantee a drug outside its recommended conditions.

When returning drugs to the laboratories, an agreement can be reached with the manufacturing laboratory, especially when the drug cost is high. The manufacturing cost is often significantly less than the most expensive selling price, and in our experience the contribution of the industry in these cases has been very adequate.

One limitation of this review is that the majority of the data found do not specify the possibility of re-refrigerating after breaking the cold chain, or whether these data are valid if there is a second break in the cold chain. For such a case, the manufacturing laboratory should be consulted.

Another limitation is that action has been formalised only for exceeding the maximum proper conservation temperature, but not for freezing.

Lastly, it is important to note that the information contained in this paper is intended as a reference tool for rapid action in those special situations when the cold chain is broken and it is necessary to know whether a drug may be used or not. If in doubt, we recommend contacting the manufacturing laboratory specifying the concrete conditions to which the product has been subjected. Due to the importance of establishing the period of time the drugs have been out of the recommended temperature range and the temperature reached, this information should not be given to other hospital departments, so as to prevent any bad conservation practice. However, it was considered appropriate to have access to it in the "*manuales de procedimiento*" section of the pharmacotherapy department portal and to inform other pharmacy departments to facilitate action in the case of a break in the cold chain. To summarise, one of

the priority functions of a pharmacist is to ensure the correct storage of medicines.¹² This requires the availability of updated information on the validity times of thermolabile drugs when the cold chain is broken. It is the responsibility of the pharmacist to establish guidelines for action when incidents occur. This information must be available and updated in the hospital pharmacy department to ensure that appropriate measures are taken.

Conflicts of Interest

The authors affirm they have no conflict of interest.

References

1. Steffen WH, Newton DW, Miller KW. Room temperature and drug stability. *Am J Hosp Pharm.* 1994;51:406-9.
2. Silgado R, Jiménez MJ, Ferrari JM, Herreros de Tejada A. Desviaciones máximas de las temperaturas permisibles para medicamentos termolábiles. *Ars Pharm.* 2006;47:173-83.
3. Cobos Campos R, Salvador Collado P, Gómez Gener A, Boj Borbones M. Estabilidad máxima de los medicamentos termolábiles fuera de nevera. *Farm Hosp.* 2006;30:33-43.
4. Bovaira García MJ, Lorente Fernández L, de la Rubia Nieto MA, San Miguel Zamora MA. Conservación de medicamentos termolábiles [s.n.]. Murcia: Hospital Universitario Virgen de la Arrixaca; 2004.
5. Sala F, Juárez JC, Tomás E, Monterde J. Estabilidad de las especialidades farmacéuticas termolábiles en distintas condiciones de temperatura: actualización. *El Farmacéutico Hospital.* 2004;160:5-16.
6. Cuervas-Mons Vendrell M, Fernández Prieto M, Sánchez Sánchez MT, Maestre Fullana MA, Abad Lecha E, Salvador Palacios A, et al. Posible validez de medicamentos termolábiles fuera de las condiciones de conservación recomendadas por el fabricante. *Farm Hosp.* 2004;28:440-4.
7. García Vázquez N, Ruano Encimar M, García López A, Arenós Monzó C, Larrubia O, Jiménez Caballero E. Estabilidad de medicamentos termolábiles a temperatura ambiente. *Farm Hosp.* 1997;21:283-8.
8. Cohen V, Jellinek S, Teperikidis L, Berkovits E, Goldman W. Room-temperature storage of medications labeled for refrigeration. *Am J Health-Syst Pharm.* 2007;64:1711-5.
9. de la Rubia A. Conservación de medicamentos termolábiles [editorial]. *Farm Hosp.* 2006;30:1-3.
10. Rivero Cava MS. Medicamentos termolábiles. *Boletín de Noticias Farmacoterapéuticas del centro de información de medicamentos y servicio de atención farmacéutica especializada de la gerencia de área de salud de Badajoz.* 2009;1:1-4.
11. Medicamentos termolábiles pauta actuación HUSD 2009 [quoted 2010 Apr 20]. *El comprimido.* Available from: http://www.elcomprimido.com/FARHSD/MP_Medicamentos_TermolabilesPautaActuacionHUSD2009.doc.
12. Ley 29/2006, de 26 de julio, de garantías y uso racional de los medicamentos y productos sanitarios. BOE núm. 178, de 27 de julio de 2006.