Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

National Cancer Control Programme

NCIS
National Cancer Information System

NCIS Training Guide

How NCIS Manages Stabilities

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Contents

1 What Stability parameters are built in NCIS?

NCIS use 4 parameters to determine the stability of final products and remainders:

- Microbiological stability of the ACU (local setting for unit)
- Physicochemical stability of the prepared product (global setting per drug product)
- Microbiological stability of remainders (local setting for unit)
- Physicochemical stability of the reconstituted vial or opened vial (global setting per drug product)

2 Can I adjust the stability assigned by NCIS?

While NCIS automatically assigns stabilities to final products and remainders the stability of each product can be altered by the end-user on a case-by –case basis in the medications edit screen.

However the final stability can never be adjusted higher than the microbiological or physicochemical stability of the remainder or opened vial. Therefore it is recommended that where a site wishes to use remainder stability this should be set to the longest stability that will ever be assigned to a final product.

3 How should we set the local stabilities?

1. Microbiological stability of the ACU should be set to the stability you usually give final products.
2. Microbiological stability of remainders should be set to the longest stability you ever give to a product.

For example if your unit gives a standard expiry of 24 hours and extends up to 7 days when required variable 1 should be set to 24 hours and variable 2 should be set to 7 days.

4 How does NCIS determine the stability of the final product?

NCIS will use the lowest of the microbiological stability of the ACU, microbiological stability of remainders or the physicochemical stability of the prepared product.

For example:

- IF ACU micro stability = 24 hours, AND Remainder micro stability = 7 days AND Product physicochemical stability = 4 hours THEN Final stability = 4 hours from time of preparation
- IF ACU micro stability = 24 hours AND Remainder micro stability = 7 days AND Product physicochemical stability = 7 days THEN final stability = 24 hours from time of preparation
- IF ACU micro stability = 7 days AND Remainder micro stability = 24 hours AND Product physicochemical stability = 7 days THEN final stability = 24 hours from time of preparation

5 How does NCIS determine the stability of remainders?

NCIS has functionality that allows remainder volumes and stabilities to be stored and used in future preparations.

NCIS uses the lowest of microbiological stability of the remainder or the physicochemical stability of the vial to determine the stability of the remainder. Only vials that require reconstitution will have a defined physicochemical stability, where available, as liquid vials have undergone no physical change.

For example:

- IF Remainder micro stability = 24 hours AND Vial physicochemical stability = 4 hours THEN remainder stability = 4 hours from time of preparation
- IF Remainder micro stability = 24 hours AND Vial physicochemical stability = 48 hours THEN remainder stability = 24 hours from time of preparation
- IF Remainder micro stability = 24 hours AND Vial physicochemical stability is not defined (liquid vial) THEN remainder stability = 24 hours from time of preparation

6 Does NCIS use remainder stabilities when determining stability of the final product?

NCIS will use the lowest of microbiological stability of the ACU, the physicochemical stability of the prepared product or the microbiological stability of the remainder to determine the stability of the final product.

Where the vial used in the final product is a reconstituted powder the physicochemical stability of the vial will not be taken into account[1]. The calculated final stability of the product can be adjusted by the end-user if required. Note: most reconstituted vials have a short physicochemical stability so are unlikely to be retained for future use (see appendix 3) therefore this scenario is unlikely in practise.

For example:

- For product made with a liquid vial:
  IF ACU micro stability = 7 days AND Product physicochemical stability = 14 days AND Remainder micro stability = 24 hours THEN final product stability = 24 hours from time of preparation of 1st product
- For product made with a powder vial:
  IF ACU micro stability = 24 hours AND Product physicochemical stability = 4 hours AND Remainder micro stability = 24 hours AND Vial physicochemical stability = 1 hour THEN final product stability = 4 hours from time of preparation of 1st product.
    - In this case the final stability may be adjusted to reflect the micro stability of the remainder as it is shorter than the physicochemical stability of the product.

7 What happens when the final concentration is outside the range in NCIS?

Concentration ranges are built into NCIS where they are specified in the SmPC for that drug. NCIS will warn you when the final concentration for the product is outside the range in the drug file; however you may ignore this warning and continue.

If you ignore the warning and choose to proceed with compounding the expiry assigned is dependent on the drug file build and will assign either of:

- 0 mins (if there are multiple stabilities for different concentrations)
- The stability assigned to the product (if there is only one concentration range)

Adjust the stability as per section 2 if required.

Note: Concentrations during verification are calculated using: dose of drug / (volume of drug + nominal fill volume). Final concentrations shown on the label are calculated based on: dose of drug / (volume of drug + actual fill volume). Appendix 4 lists the infusions solutions built in NCIS with their corresponding fill volumes.

[1] The physicochemical stability of the vial is not taken into account as this will be used as the final stability of the product if it is the shortest expiry. This can lead to situations where the final product stability is artificially short. For example Decitabine has a vial stability of 15 minutes but the final stability of the product is 5 hours. If the vial stability was taken into account NCIS would assign a final stability of 15 minutes.

Appendix 1 – Testing Scenarios

Final Product Stability Using Original Vials

ACU Stability	Product Physicochemical Stability	Remainder Micro stability	Vial Physicochemical Stability	Ignore vial stability	Expected Result	Achieved Result
24 hours	4 hours	24 hours	Nil	Yes	4 hours	4 hours
24 hours	7 days	24 hours	Nil	Yes	24 hours	24 hours
24 hours	7 days	4 hours	Nil	No	4 hours	4 hours
24 hours	7 days	4 hours	2 hours	No	2 hours	2 hours
24 hours	7 days	4 hours	2 hours	Yes	24 hours	24 hours

Final Product Stability Using Remainders

ACU Stability	Product Physicochemical Stability	Remainder Micro stability	Vial Physicochemical Stability	Ignore vial stability	Expected Result	Achieved Result
24 hours	4 hours	2 hours	1 hour	Yes	4 hours from 2nd prep	4 hours from 2nd prep
24 hours	4 hours	2 hours	Nil	Yes	4 hours from 2nd prep	4 hours from 2nd prep
24 hours	7 days	2 hours	Nil	Yes	24 hours from 2nd prep	24 hours from 2nd prep
24 hours	4 hours	24 hours	Nil	Yes	4 hours from 2nd prep	4 hours from 2nd prep
7 days	14 days	24 hours	Nil	No	24 hours from 1st prep	24 hours from 1st prep
7 days	14 days	24 hours	4 hours	No	4 hours from 1st prep	4 hours from 1st prep

Remainders Stability

ACU Stability	Product Physicochemical Stability	Remainder Micro stability	Vial Physicochemical Stability	Ignore vial stability	Expected Result	Achieved Result
24 hours	7 days	24 hours	4 hours	Yes	4 hours	4 hours
24 hours	7 days	24 hours	2 days	Yes	24 hours	24 hours
24 hours	4 hours	24 hours	Nil	Yes	24 hours	24 hours
24 hours	2 hours	24 hours	4 hours	Yes	4 hours	4 hours

Final Product Stability Using Original Vials with limited expiries

Lot expiry (vial)	Lot expiry (fluid)	ACU Stability	Product PC Stability	Remainder Micro stability	Vial PC Stability	Ignore vial stability	Expected Result	Achieved Result
24 hours	3 days	7 days	14 days	7 days	3 days	No	Lot expiry vial	Lot expiry vial
3 days	24 hours	7 days	14 days	7 days	2 days	No	Lot expiry infusion fluid	Lot expiry infusion fluid

Remainder Stability

Lot expiry (vial)	Lot expiry (infusion fluid)	ACU Stability	Product PC Stability	Remainder Micro stability	Vial PC Stability	Ignore vial stability	Expected Result	Achieved Result
24 hours	3 days	7 days	14 days	7 days	3 days	No	Lot expiry vial	Lot expiry vial
3 days	24 hours	7 days	14 days	7 days	2 days	No	2 days	2 days

Final Product Stability with Deviating Stability

ACU Stability	Product Physicochemical Stability	Remainder Micro stability	Vial Physicochemical Stability	Deviating Stability	Expected Result	Achieved Result
7 days	14 days	24 hours	Nil	28 days	24 hours	24 hours
7 days	14 days	7 days	Nil	28 days	7 days	7 days
24 hours	14 days	7 days	Nil	28 days	7 days	7 days
24 hours	14 days	24 hours	Nil	28 days	24 hours	24 hours
24 hours	14 days	Blank	Nil	28 days	28 days	28 days
24 hours	14 days	7 days	Nil	4 hours	4 hours	4 hours
24 hours	14 days	7 days	4 hours (do not ignore)	28 days	4 hours	4 hours
24 hours	14 days	7 days	4 hours (ignore)*	28 days	28 days	28 days
24 hours	4 hours	7 days	Nil	27 days	7 days	7 days

* Powder vial setup

Appendix 2 – Master Data Settings

Master Settings:

Consider Stability of Remainders: *Should the stability of used remainders be considered when the stability of the finished preparation is calculated?* – Yes

Dosage Forms of a Product - Settings:

Vial type	Reconstituted/opened Stability (vial stability)	Ignore stability of the opened product for the stability of the medication (ignore vial stability)
Liquid	No	No
Powder	Yes (where available)	Yes

Appendix 3 – Stabilities of powder vials in NCIS

Active ingredient	Product	Physicochemical stability of vial	Physicochemical stability of prepared final product
Abatacept	Orencia Powder for solution for infusion	24 hours	24 hours
azaCITIDine	Vidaza Powder 15-25 deg WFI, 15-25 deg storage, 45min exp	45 minutes	45 minutes
azaCITIDine	Vidaza Powder 15-25 deg WFI, 2-8 deg storage, 8h exp	8 hours	8 hours
azaCITIDine	Vidaza Powder 2-8 deg WFI, 2-8 deg storage, 22h exp	22 hours	22 hours
Bendamustine	Bendamustine Actavis Powder for solution for infusion	Nil available	2 days
Bendamustine	Bendamustine Accord Powder for solution for infusion	Nil available	2 days
Bleomycin	Bleo-Kyowa Powder for solution for injection	72 hours	24 hours
Blinatumomab	Blincyto Powder for solution for infusion	**24 hours**	96 hours
Bortezomib	Velcade Powder for intravenous use	8 hours	8 hours
Bortezomib	Velcade Powder for subcutaneous use	8 hours	8 hours
Brentuximab vedotin	Adcetris Powder for solution for infusion	24 hours	24 hours
Cabazitaxel	Jevtana Concentrate for solution for infusion	**1 hour**	48 hours
Carfilzomib	Kyprolis Powder for solution for infusion	24 hours	24 hours
Crisantaspase	Erwinase Powder for solution for injection	**15 minutes**	4 hours
Cyclophosphamide	Endoxana Powder for solution for injection	**48 hours**	7 days
Dacarbazine	Dacarbazine medac Powder for solution for injection/infusion 100 mg and 200 mg	24 hours	24 hours
Dacarbazine	Dacarbazine medac Powder for solution for infusion 500 mg	Nil available	24 hours
DACTINomycin	Cosmegen Lyovac Powder for solution for injection	10 hours	10 hours

Active ingredient	Product	Physicochemical stability of vial	Physicochemical stability of prepared final product
DAUNOrubicin	Cerubidin Powder for solution for infusion	**24 hours**	14 days
Decitabine	Dacogen Powder for solution for infusion	**15 minutes**	5 hours
Fludarabine	Fludara Powder for solution for injection/infusion	7 days	7 days
Ganciclovir	Cymevene Powder for solution for infusion	**12 hours**	185 days in NaCl 0.9%; 24 hours in G5%
IDArubicin	Zavedos Powder for solution for injection	24 hours	24 hours
Ifosfamide	Mitoxana Powder for solution for injection/infusion	Nil available	8 days
Melphalan	Alkeran Powder for solution for infusion	1 hour	1 hour
Mifamurtide	Mepact Powder for dispersion for infusion	6 hours	6 hours
mitoMYcin	mitoMYcin-C Kyowa Powder for solution for injection	Nil available	4 hours
PACLitaxel albumin bound	Abraxane Powder for suspension for infusion	24 hours	24 hours
Pembrolizumab	Keytruda Powder for solution for infusion	24 hours	24 hours
PEMEtrexed	Alimta Powder for solution for infusion	24 hours	24 hours
Pentostatin	Nipent Powder for solution for injection/infusion	8 hours	8 hours
Pixantrone	Pixuvri Powder for solution for infusion	Nil available	24 hours
Siltuximab	Sylvant Powder for solution for infusion	**2 hours**	6 hours
Temsirolimus	Torisel Concentrate for solution for infusion	**24 hours**	6 hours
Thiotepa	Tepadina Powder for solution for infusion	**8 hours**	24 hours
Topotecan	Hycamtin Powder for solution for infusion	Nil available	7 days
Trastuzumab	Herceptin intravenous Powder for solution for infusion	**48 hours**	30 days

Active ingredient	Product	Physicochemical stability of vial	Physicochemical stability of prepared final product
Trastuzumab emtansine	Kadcyla Powder for solution for infusion	24 hours	24 hours

Expiries in Bold indicate vial stability less than final product stability

Appendix 4 – Infusion Solution Volumes

Infusion Solution	**Nominal Fill Volume**	**Actual Fill Volume**	**Max Filling Volume**
50mL Viaflo bag non-PVC Baxter (NaCl 0.9% & glucose 5%)	50.00mL	59.00mL	130.5mL
100mL Viaflo bag non-PVC Baxter (NaCl 0.9% & glucose 5%)	100.00mL	111.00mL	177.00mL
250mL Viaflo bag non-PVC Baxter (NaCl 0.9% & glucose 5%)	250.00mL	271.00mL	417.00mL
500mL Viaflo bag non-PVC Baxter (NaCl 0.9% & glucose 5%)	500.00mL	530.00mL	795.00mL
1000mL Viaflo bag non-PVC Baxter (NaCl 0.9% & glucose 5%)	1000.00mL	1047.00mL	1236.50mL
50mL Freeflex bag non-PVC Fresenius Kabi (NaCl 0.9%)	50.00mL	53.00mL	123.00mL
100mL Freeflex bag non-PVC Fresenius Kabi (NaCl 0.9%)	100.00mL	103mL	153.00mL
250mL Freeflex bag non-PVC Fresenius Kabi (NaCl 0.9% & glucose 5%)	250.00mL	253.00mL	328.00mL
500mL Freeflex bag non-PVC Fresenius Kabi (NaCl 0.9% & glucose 5%)	500.00mL	503.00mL	653.00mL