National Cancer Control Programme

National Cancer Information System

NCIS GUIDE

How NCIS Manages Stabilities

Contents

1 What Stability parameters are built in NCIS?

Stability of final Products is managed in the Preparation Module of NCIS.Med (BD CATO)

BD CATO use four 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.Med?

While NCIS.Med 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, as shown below

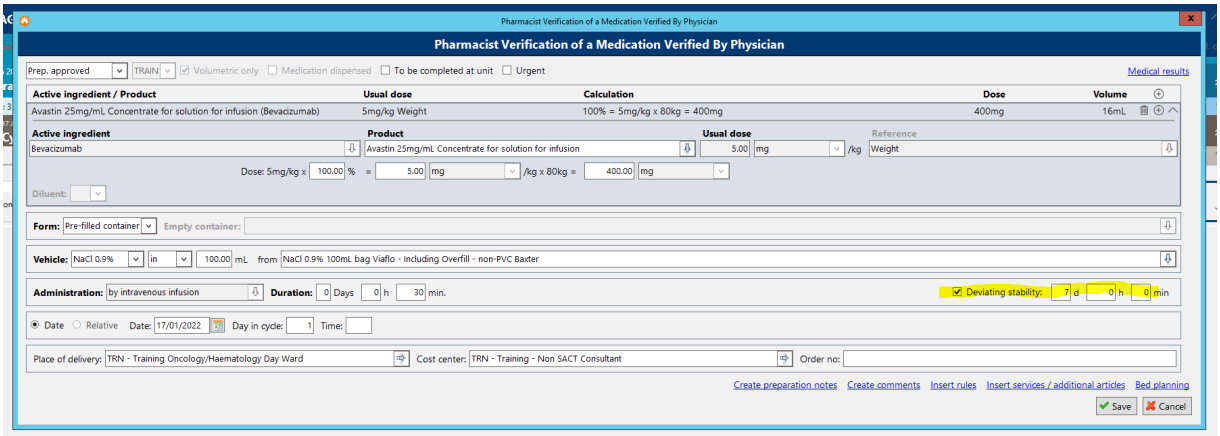


Figure 1: Pharmacist Verification Window, highlighting deviating stability

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. Or if your unit never gives longer than 24 hours, both stabilities should be set to 24 hours.

4 How are physicochemical stabilities in the drug file determined?

Stability information in NCIS.Med is added at Dosage Forms of a Product level and can be broken down by vehicle and concentration. This information is visible to NCIS_pharmacist and NCIS_pharmacy_technician users in Master Data > Dosage Forms of a Product.

As noted above the stabilities displayed in BD CATO are suggestive only and may be adjusted by individual sites at an individual preparation level based on local procedures.

The following reference sources were agreed by the PCAG (Pharmacy Compounding Advisory Group) as valid for building stability in the drug file:

- SmPC Data
- Company Data (which may not be in the SmPC)
- Data from Stabilis.org that is rated A or A+
- Other stability reference data published in peer reviewed journals

Notwithstanding the agreed reference sources, other stability summary information may also be consulted, as a basis for comparison, for example:

- Specialist Pharmacy Services
- BCCA drug monograph stability

Where stability data from the above reference sources is conflicting or impractical the NCIS office will invite expert opinion and may also liaise with the manufacturer for additional information on the appropriate stability to build in the drug file.

The final stability included in the NCIS build is determined by the NCCP Regimen team.

- Stability decisions are made at the NCCP Regimen Team meeting when at least two of either NCCP Chief II or Chief I Pharmacists are present
- The references used to determine the final stability in the NCIS drug file are included in the remarks section in Master Data > Dosage Forms of a Production

The physicochemical stability information that is used to calculate final stability can be viewed in the Stability Tab of dosage forms of a product, as shown below:

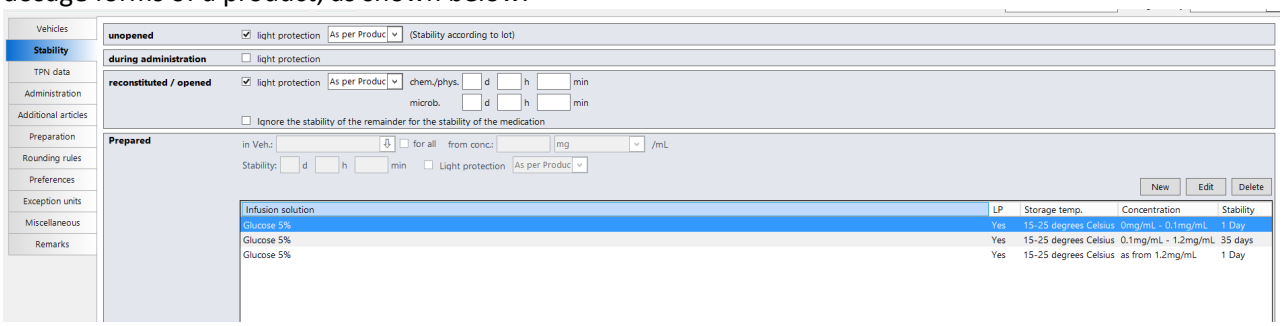


Figure 2: Stability Tab of Dosage Forms of a Product

5 How does NCIS.Med 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

6 How does NCIS.Med 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 entered in the NCIS Drug File, 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

7 Does NCIS.Med 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 unless it is greater than or equal to 7 days. 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.Med would assign a final stability of 15 minutes. 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 therefore this scenario is unlikely in practice. However if the vial has a physicochemical stability greater than or equal to 7 days it may be shared so for these specific products the vial stability is considered and will not impact microbiological stability as this is generally not greater than 7 days. For physicochemical stability of reconstituted powder vials see Master Data > Dosage Forms of a Product > Stability > Reconstituted/Opened.

For example:

- For product made with a liquid vial remainder:
  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 remainder with physiochemical stability <7days (see footnote 1):
  IF ACU micro stability = 7 days AND Product physicochemical stability = 24 hours AND Remainder micro stability = 4 hours AND Vial physicochemical stability = 1 hour THEN final product stability = 24 hours from time of preparation of 2nd product.
    - In this case the final stability may be adjusted to reflect the micro stability or physicochemical stability of the remainder as they are both shorter than the physicochemical stability of the product.
- For product made with a powder vial remainder with physiochemical stability ≥7 days:
  IF ACU micro stability = 7 days AND Product physicochemical stability = 30 days AND Remainder micro stability = 4 hours AND Vial physicochemical stability = 7 days THEN final product stability = 4 hours from time of preparation of 1st product.

8 What happens when the final concentration is outside the range built in NCIS.Med?

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.

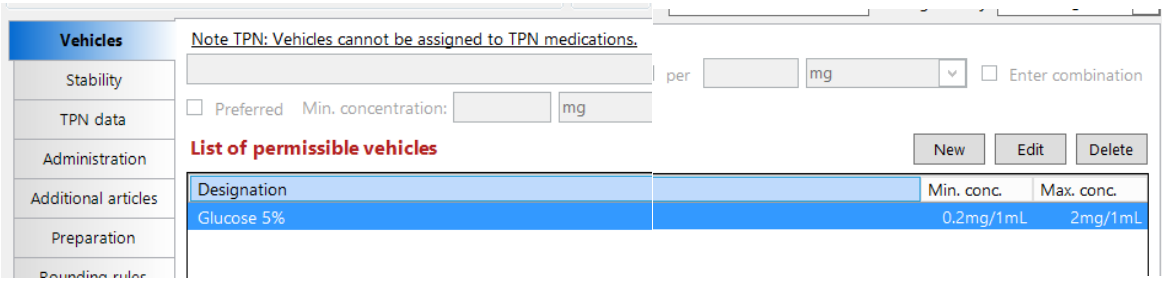


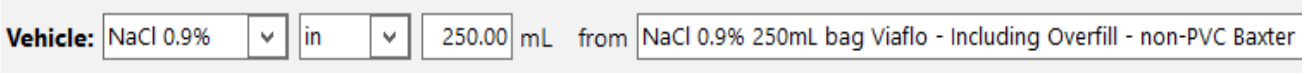
Figure 3: The vehicles tab in Dosage Forms of a Product shows concentration ranges for vehicles. For example this product can only be diluted in Glucose 5% and a warning will be triggered if the concentrations is <0.2mg/mL or >2mg/mL

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 and the concentration of the final product falls outside the ranges for which a stability has been defined)
- 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), the reason is that when the product is being pharmacist verified the vehicle will always be verified 'in' the nominal fill volume, see below, therefore the system will calculate the concentration using the nominal fill volume. If the drug the volume is specified exactly with q.s. then this is the volume that will be used at all points in the process.



Final concentrations shown on the label are calculated based on: dose of drug / (volume of drug + actual fill volume). Infusion volumes built in the NCIS Drug file are visible in Master Data > Infusion Solutions and are based on information provided by the infusion fluid manufacturer.

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 (physicochemical vial stability)	Ignore stability of the opened product for the stability of the medication (ignore vial stability)
Liquid	Field left blank	No
Powder with physicochemical stability <7 days	Physicochemical stability of vial entered (where available)	Yes
Powder with physicochemical stability ≥7 days	Physicochemical stability of vial entered (where available)	No