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1. Technical guide – barcode labelling on primary and secondary packages for pharmaceutical products

1.1 Preface

This technical guide was developed to help companies put correct barcodes on primary and secondary packages in order to meet the requirements for delivering pharmaceuticals to public hospitals in Denmark.

1.2 Definition of primary package and secondary package

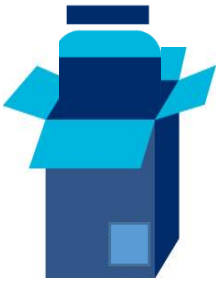
The primary package (inner package) – the first level of packaging for the product marked with a barcode either on the packaging or on the label affixed to the packaging. The first level of packaging is the packaging in direct contact with the product.

Figure 1: Examples of primary packages

If the primary package is not contained in a box and thereby also constitutes the secondary package, the requirements for a barcode symbol on a secondary package must be complied with.

Secondary package (outer package) – A level of packaging marked with a barcode that may contain one or more primary packages or a group of primary packages containing a single item.

Figure 2: Examples of secondary packages



1.3 Questions which can occur when labelling the products

1. Is it okay to have the same GTIN on the primary package and the secondary package?
    a. Yes, if they share a "one-to-one" relationship → For more information see paragraph 2.6
    b. No, not if you need to clearly differentiate between primary and secondary packages → For more information see paragraph 2.6
    c. No, not if the secondary package contains two or more primary packages → For more information see paragraph 2.6
2. Must the primary packages of the same trade item always have the same GTIN?
    a. Yes, for more information see paragraph 2.6
3. What is the difference between NTIN and GTIN?
    a. See paragraph 2.4
4. What is the difference between a linear barcode and a 2D barcode?
    a. See paragraph 3
5. Which changes must be carried out to comply with the new regulations on serialization?
    a. See paragraph 4

2. Identification of pharmaceuticals

2.1 Allocation of Nordic Article Number (Vnr)

When a pharmaceutical product has a marketing license, the holder of the marketing license or the representative of this must request a Nordic Article Number (Vnr) from the Pharmaceutical Information Center (PIC) in Finland https://vnr.fi/.

An assigned Vnr must only be used for one marketing license.

https://www.retsinformation.dk/pdfPrint.aspx?id=182152 (Text in Danish)

The package must have a barcode containing a unique ID-number, which by scanning provides access to a database with information about the pharmaceutical product.

The manufacturer can use a NTIN or a GTIN.

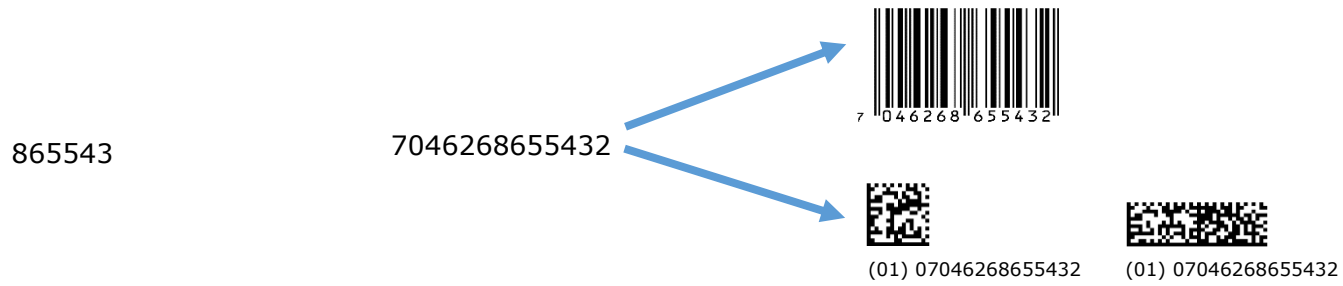
2.2 NTIN (National Trade Item Number)

A NTIN is a coding scheme, administered by PIC in Finland for which a prefix has been issued to permit its uniqueness within the GS1 pool, but without assurance of the full compatibility with GTIN functionality. In Denmark and the other Nordic countries, the number begins with the Nordic prefix "704626" followed by the Vnr and ends with a check digit[1].

[1] The check digit is calculated based on the first 12 numbers. The check digit can be calculated on http://www.gs1.dk/support/beregn-dit-kontrolciffer/

The Nordic prefix must be requested through PIC in Finland; however, as of February 2019 it will no longer be possible to assign a Nordic prefix to new pharmaceutical products.
The allocation rules for these Nordic NTINs follow the Danish Medicines Agency allocation rules for Vnr. If the name of the product changes, then the Vnr changes, and therefore the NTIN.

Figure 3: The link between Vnr, NTIN and barcode symbol



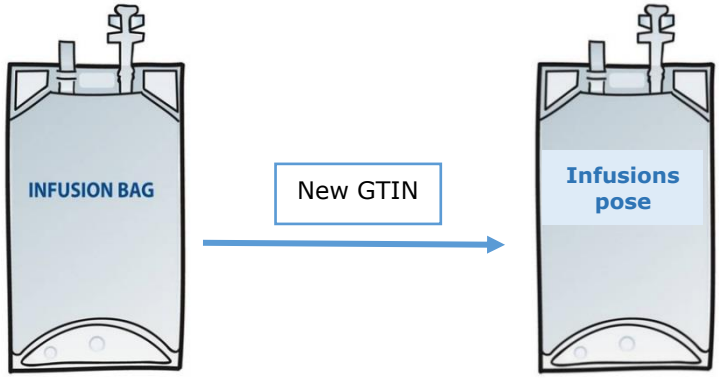
Note: When a 13-digit NTIN is put in a GS1 DataMatrix, remember to add a leading zero, as the predefined length for Application Identifier (01) in a GS1 DataMatrix is 14 digits: e.g. 074676268655432.

2.3 GTIN (Global Trade Item Number)

A GTIN is the GS1 identification key used to identify trade items. The key comprises a GS1 Company Prefix, an item reference and check digit. A GTIN is acquired through a membership of GS1 Denmark or another GS1 member organization. GTIN works as a key to a database, where information about the product can be found [1]. Allocation of GTINs follows the GS1 allocation rules [2]. If a product changes significantly, it requires a new GTIN.

Figure 4: Examples of assigning a new GTIN

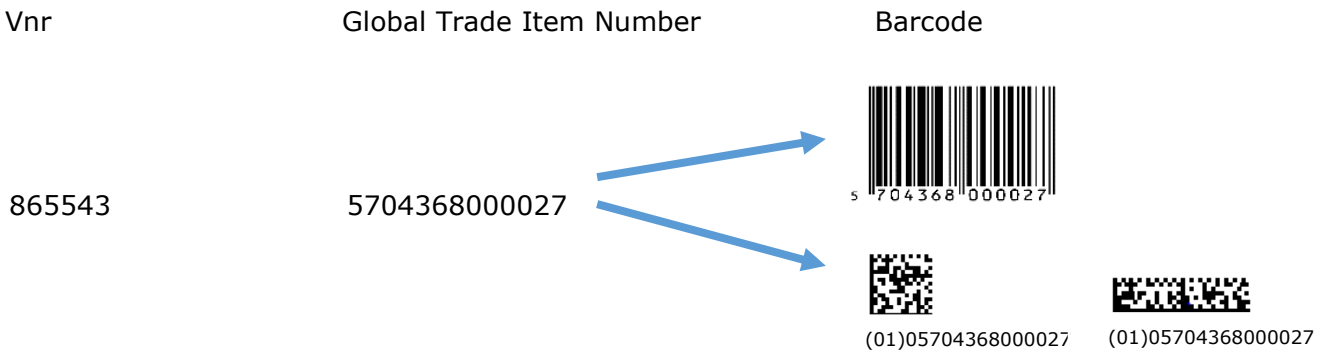
The language on the product changes



The pack size changes

The above shown are just examples of when to assign a new GTIN to the product. To get a complete overview of the GTIN allocation rules, se GS1 Healthcare Allocation Rules [2].

Figure 5: The link between Vnr, GTIN and barcode symbol



Note: When a 13-digit GTIN is encoded in a GS1 DataMatrix, remember to add a leading zero, as the predefined length for Application Identifier (01) in a GS1 DataMatrix is 14 fields: 057043680000327.

2.4 The difference between NTIN and GTIN

NTIN is created from a national number, which can be encoded in a GS1 barcode and used in processes, but its assignment is controlled by a third party outside of GS1. GTIN is a globally unique number, which identifies products based on GS1 standards.

NTIN follows the allocation rules for Vnr, and changes only when the Vnr changes, whereas the allocation rules for GTIN are different. An example: if the packaging of a pharmaceutical product changes from a blister pack to a pill bottle. In this example, the Vnr will remain the same, which means that the NTIN will not change. However, this change in packaging will result in a new GTIN.

Figure 6: Example of the difference between NTIN and GTIN

A pharmaceutical product distributed to Denmark, Norway and Sweden with leaflets in Danish, Norwegian and Swedish, respectively can have the same Vnr and then the same NTIN. However, the three packages will have three different GTINs (see figure 7).

Figure 7: A pharmaceutical product with three different leaflets can have the same NTIN, but must have different GTINs

Country	Vnr	NTIN	GTIN
Denmark	123456	7046261234569	5712345000014
Norway	123456	7046261234569	5712345000021
Sweden	123456	7046261234569	5712345000038

2.5 transition from NTIN to GTIN

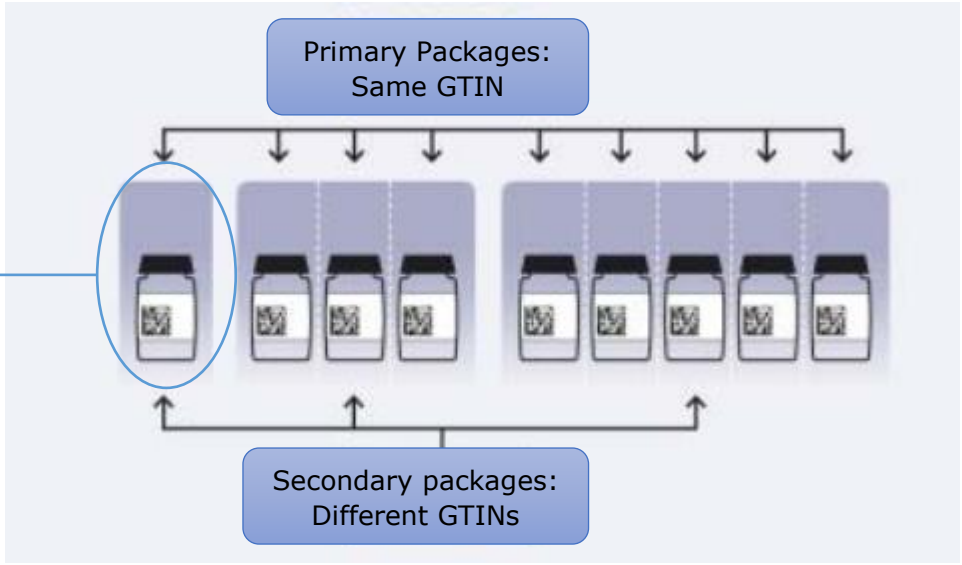
If the manufacturer wants to change from NTIN to GTIN, it is important to inform the trading partners, so that the number can be changed in their databases. Note that the change from NTIN to GTIN can cause challenges in the supply chain, since not all systems today can handle multiple data fields per Vnr.

2.6 Allocation of GTINs to primary and secondary packages

It is important that one GTIN identifies one product, and that a given product only has one GTIN.

Primary packages must retain the same GTIN even though there are different quantities of primary packages within secondary packages, see figure 8.

Figure 8: Every pill bottle has the same GTIN, however, the different secondary packages have different GTINs



Some healthcare processes require the capability to clearly differentiate between a healthcare trade item and its primary and secondary packaging or "packaging hierarchy", even if they share a 1:1 relationship. In this situation, the trade item primary package and secondary package may have different GTINs assigned.

2.7 When pharmaceutical products consist of powdered medication and a diluent

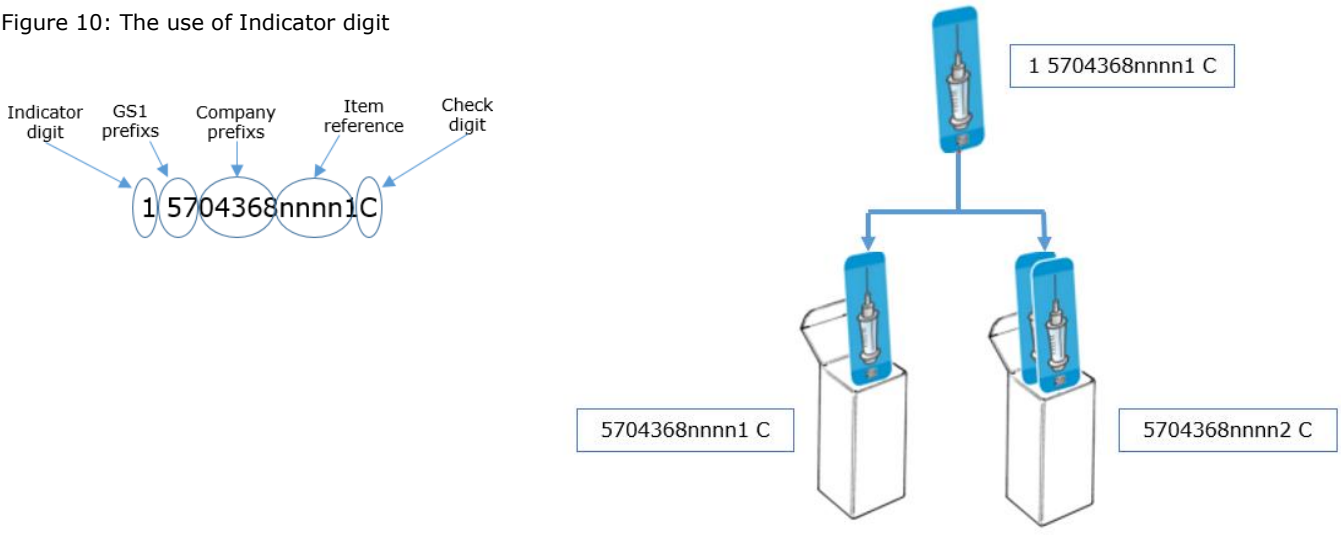
Some pharmaceutical products consist of powdered medication and a diluent. Amgros does not require barcodes on the diluent, however, it is allowed. Since the secondary package contains two vials, it is not a 1:1 relationship, and the vial with the powdered drug must have a GTIN, and the package, which contains the powered drug + the diluent, must have another GTIN, see figure 9.

Figure 9: Allocation of GTINs to packages which contain powdered drug + diluent

2.8 Indicator digit

The Indicator is a digit with a value of 1 to 8, which is placed in front of the GTIN-13 or NTIN-13. Hereby, a GTIN-14 or NTIN-14 is constructed. The manufacturer or supplier has the option of either assigning a unique GTIN-13 to each packaging level or a unique GTIN-14 with an indicator, see figure 10.

Figure 10: The use of Indicator digit



Note, that the check digit for each variant is re-calculated, see figure 11.

Figure 11: Indicator digit used to identify different packaging levels (not logistic units)

Indicator digit	GTIN less check digit	Check digit	Description	Quantity
	570436800001	**0**	Secondary package	A box with X
1	570436800001	**7**	Primary package	1 item
2	570436800001	**4**	Case	A case containing 10 secondary packages
3	570436800001	**1**	Pallet	A pallet with 10 cases
…	…	**…**	…	…
8	570436800001	**6**	Standard trade item grouping	A grouping of products
Indicator 1 to 8 can be used to create new GTIN-14s (Indicator digit 9 is reserved for Variable Measure Trade items).				

3. Barcode type, content and dimensions

3.1 EAN-13

EAN-13 contains only a 13-digit item number (NTIN/GTIN), see figure 12.

Figure 12: Example of EAN-13 barcode symbol

Dimensions:

When used the EAN-13 barcode symbol must not be smaller than 6 x 19 mm. An EAN-13 barcode, which measures 6 x 19 mm and can be scanned by the hospital's scanners is analogues to the barcode symbol on SAD vial labels.

Note: Amgros allows barcode dimensions of 6 x 19 mm for the EAN-13 barcode, which is a more truncated height than GS1 General Specification recommendation.

Quiet Zones:

It is important for the scanning process that there is a margin on both sides of the barcode – called a quiet zone, which contains no text or other information or graphics. The quiet zone

defines where the barcode begins and where it ends. The size of the quiet zone depends on the dimensions of the barcode [1].

3.2 GS1 DataMatrix

The GS1 DataMatrix barcode symbol is by definition a version of ISO/IEC 16022 DataMatrix with a Function Code 1 (FNC1) character in the first data position. This indicates to the scanner that the data that has been decoded is in a GS1 data format. The GS1 General Specifications describes the data formats with which the different types of information contained in the barcode must comply.

A GS1 DataMatrix can contain more information than just the GTIN (or NTIN) for example a batch/lot number, serial number and/or expiration date.

Figure 14: Example of GS1 DataMatrix containing GTIN, Expiration date, Batch/Lot number and Serial number

(01)05704368000027(17)160327

(10)ABC123(21)123

Note: The parentheses must not be a part of the encoded data in the barcode, but are only a part of the human readable text.

Dimensions:

A GS1 DataMatrix has two formats – a square format and a rectangular format. It depends on e.g. the size and shape of the product, amount of data to encode and the printing process which format is suitable for the product.

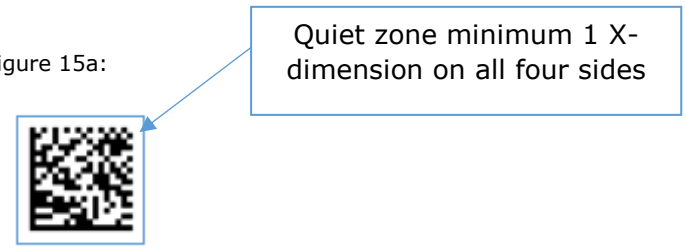
The minimum module dimension for a GS1 DataMatrix in this application is an X-dimension of 0.255 mm, where the X-dimension refers to height and width of a single module (square/dot) in a GS1 DataMatrix. Maximum X-dimension in this application is 0.495.

Figure 15: Minimum dimensions of a GS1 DataMatrix only containing a GTIN, and an X-dimension of 0.255mm

Quite Zones:

The dimension of the Quite Zone for a GS1 DataMatrix is 1 X-dimension on all four sides, see figure 15a (3).

Figure 15a:

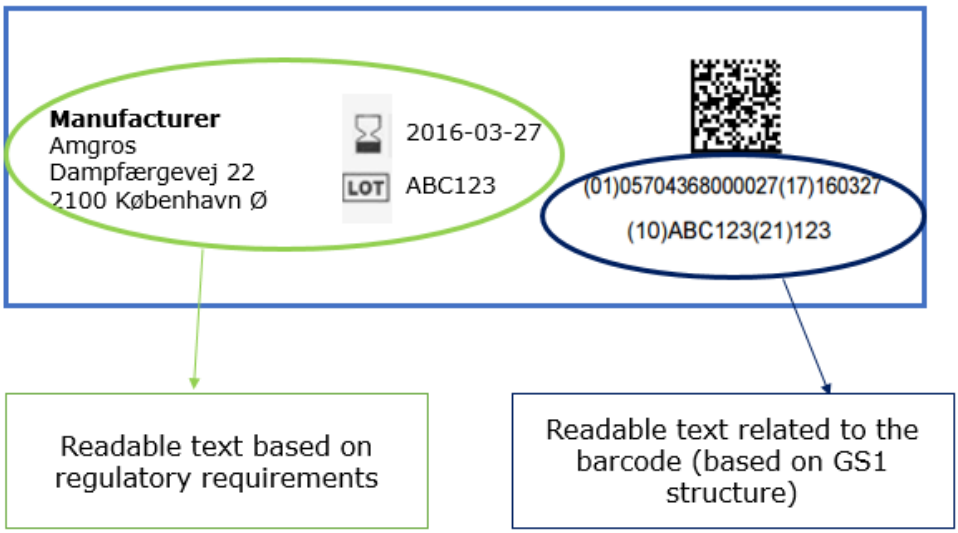


3.2.1 Human readable interpretation

There are two formats of human readable text. The text related to the encoded data within the barcode ("human readable interpretation" or HRI), and all other text on the label ("non-HRI text"), which may be based on regulatory requirements, see figure 16.

The HRI for the data encoded within the barcode shall always be printed adjacent to the GS1 barcode, while protecting the quite zones. In circumstances with extreme space constrains it is possible to leave out some of the readable text related to the barcode, however, if possible it is important to have the GTIN in readable text [1].

Figure 16: Example of a label containing a GS1 DataMatrix, human readable interpretation and non-HRI text:



4. Serialization

The deadline for implementation of the Falsified Medicines Directive is the 9th of February 2019, which means that all pharmaceutical products for prescription on the European market, must be uniquely identified. The sales unit must have a 2D barcode, which can be a GS1 DataMatrix where GTIN, serial number, batch number and expiry date are encoded. The

requirements are only applicable to sales units, and not the other packaging levels [4]. See figure 17.

Figure 17: Primary and secondary packages before and after 2019

Primary packages **before** and **after** 2019

Secondary packaging **before** 2019

Secondary packages **after** 2019

Example:

(01) = GTIN

(17) = Expiration date

(10) = Batch/Lot number

(21) = Serial number

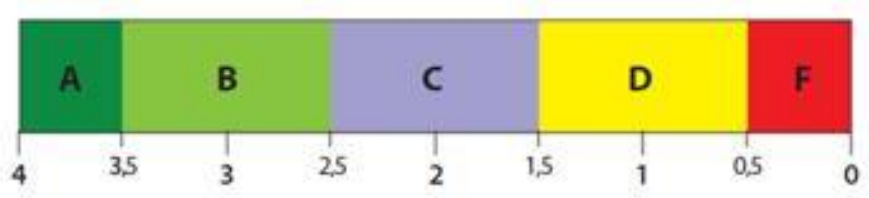
To see the formats of GTIN, expiration date, batch/lot number and serial number, see Appendix.

5. Barcode Quality

Barcode symbols must be scannable at a satisfying level of performance through the expected life span of the product and through the whole supply chain. ISO/IEC 15416 defines a standardised methodology for measuring and grading linear barcodes like EAN-13, and ISO/IEC 15415 describes the standard for measuring and grading GS1 DataMatrix. The standards use a reporting system, which expresses the overall symbol grade by a digit between 0 and 4 or a letter between A and F.

According to GS1 General Specifications, both an EAN-13 and a GS1 DataMatrix must at least have an overall symbol grade of 1,5/C [1].

Figure 18: Quality Scale with both letters and digits



The Manufacturers who apply barcode symbols are responsible for meeting symbol quality requirements. Different types of equipment for testing the symbol quality of the barcode are available, and it is important that the equipment also complies with all applicable standards [5,6,7].

Note: It is recommended to test the quality of the barcode symbol in its final configuration, such as when the label is on the product to ensure that noted quality is representative of how it will be perceived within the supply chain.

6. General placement rules

It is recommended that the barcode is placed on a plane surface and never around a corner, on a rim, at a welding seam or the like that will hinder or obscure the scanning of the symbol [1]. If the barcode is placed on a curved surface with a diameter less than 6 cm, it is recommended to have the EAN-13 barcode symbol in ladder orientation.

For GS1 DataMatrix, it is necessary that the scanner can image or "take a picture" of the whole barcode. To increase scannability it is recommended to place the GS1 DataMatrix on a plane surface (e.g. top or bottom of the product), so that the barcode is not distorted or changed in size or shape or color, see figure 19.

Figure 19:

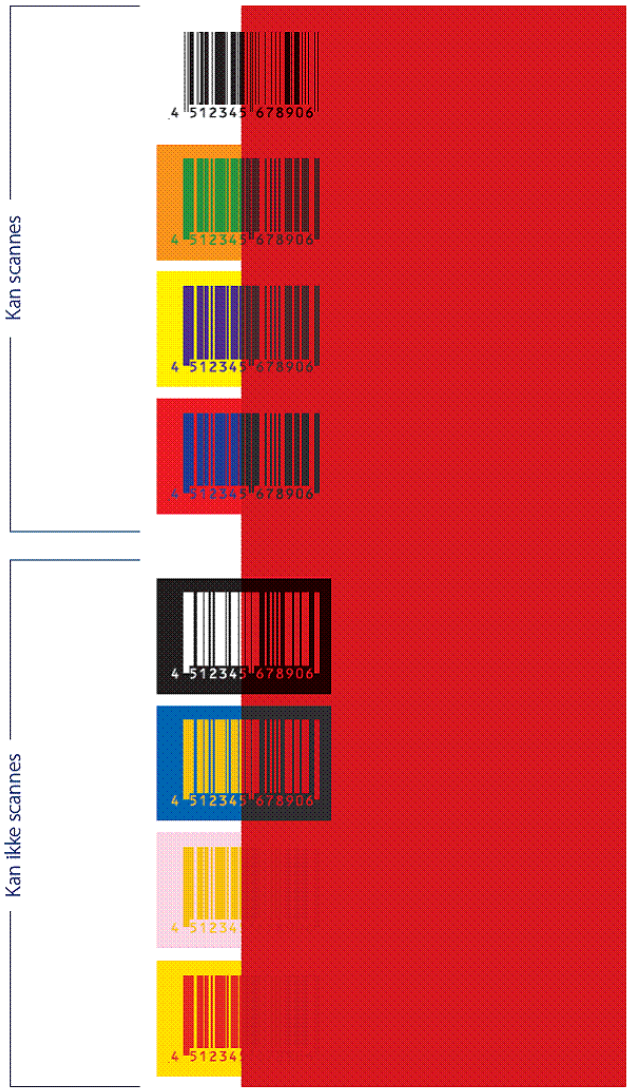
7. Color and contrast

Scanners rely on the reflective contrast between the dark bars and light spaces (on a linear symbol like an EAN-13) to properly "see" and read the barcode.

To obtain maximum contrast it is recommended to print black lines on a white background. As a general rule, red, orange and yellow can be used as background. Dark colors like black, blue and green are considered useful for the dark bars in the barcode, see figure 20.

Scanning of 2D barcodes uses image-technology. The same rules of maximum contrast are applicable, however, the option does exist to use light modules on a dark background.

Figure 20: Examples of color combinations in linear barcodes which give maximum contrast, and examples of color combinations, which will generally not be scannable or provide very poor performance.



8. Barcode label printing and environment

If a barcode label is used it is important to use a substrate material and an adhesive that suits the environment (e.g. humidity, cold, hot and room temperature) so the barcode is scannable throughout its life span and the label will not deteriorate and/or fall off.

If a barcode is printed directly on the product, it is important to use ink that in conjunction with the packaging material suits the environment (e.g. cold, hot and room temperature) so the barcode always is scannable.

9. Information about primary package identification to trading partners

A GTIN on the primary package must be linked to the product information on the secondary package. In the hospital sector, this is achieved by Amgros receiving the necessary information from the manufacturer or the marketing license holder and making this information available in a pharmaceutical database. The database is made accessible for hospital trading partners.

10. Information about secondary package identification to trading partners

The secondary package, which is the sales unit, has a GTIN or NTIN and a Vnr. All related product information is linked to the Vnr and is communicated through Medicinpriser.dk. The database is accessible to hospital trading partners.

11. Amgros communication of product information to public hospitals

Information about GTIN on primary packages must be registered on Amgros' Leverandør- og Udbudsportal (Supplier and Tendering site) [8].

ApoVision, which is the system behind the hospitals' dose dispensing, EHR / EPM, etc., will also redistribute GTIN information on primary packages for use in wards, clinics and service production and other places in which safe pharmaceutical identification should take place.

12. References

1. GS1 General Specifications
   (http://www.gs1.org/docs/barcodes/GS1_General_Specifications.pdf)
2. GS1 Healthcare GTIN Allocation Rules
   (http://www.gs1.org/docs/gsmp/healthcare/GS1_Healthcare_GTIN_Allocation_Rules.pdf)
3. GS1 DataMatrix Guideline
   (http://www.gs1.org/docs/barcodes/GS1_DataMatrix_Guideline.pdf)
4. Commission delegated regulation (EU) 2016/161
   (http://ec.europa.eu/health/files/eudralex/vol-1/reg_2016_161/reg_2016_161_en.pdf)
5. ISO/IEC 15416 Information technology — Automatic identification and data capture
   (http://www.iso.org/iso/catalogue_detail?csnumber=27659)
6. ISO/IEC 15415 Information technology — Automatic identification and data capture
   (http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=54716)
7. ISO/IEC 15426 Information technology — Automatic identification and data capture techniques — Bar code verifier conformance specifications — Part 1: Linear symbols / Part 2: Two-dimensional symbols
   (http://www.iso.org/iso/catalogue_detail.htm?csnumber=57022)
8. Amgros
   http://www.levportal.amgros.dk

13. Appendix: Data structure for GS1 DataMatrix

Data in a GS1 DataMatrix barcode must comply with the GS1 data structure as noted in the GS1 General Specifications [1]. This encoded data structure must always begin with a FNC1 character. The FNC1 character is used to indicate to the decoding software that the data in the barcode has been encoded per the rules of the GS1 General Specifications.

This data format schema may contain many different types of information. The most commonly used types of information in healthcare is GTIN, batch/lot number, expiration date and serial number.
Information is expressed in the form of Application Identifiers (AI) followed by the data. An Application Identifier is a number consisting of 2-4 digits, which indicates to the software processing the decoded data from the barcode scanner the meaning and format of the characters after the AI.

Table: Data formats for GTIN, batch number, expiry date and serial number

Application Identifier	Information type	Data format
01	GTIN (product number)	n2+n14
10	Batch number	n2+an…20
17	Expiration date - YYMMDD	n2+n6
21	Serial number	n2+X…20

Explanation of table information:
n2: how many digits must be within the parenthesis
n14: how many digits must be after the closing parenthesis
X...20: the batch and serial number can be both letters and numbers and up to 20 digits.

Example for data formatting:
GTIN: 5702830382244
Exp. date: 180901 = September 1, 2018
Batch number: BV1234
(01)05702830382244(17)180901(10)BV1234

Note:
When encoding data into certain GS1 barcodes (e.g. GS1 DataMatrix), a GTIN must be expressed as a 14-digit number. If the assigned GTIN is a GTIN-8, GTIN-12 or GTIN-13, respectively four, two and one leading zero must be added.

Application Identifier (10) – batch or lot number:

The application Identifier (10) indicates that the data field contains a batch or lot number. The batch or lot number associates an item with information the manufacturer considers relevant for traceability of the trade item to which the element string is applied. The number may be for example, a production lot number, a shift number, a machine number or a time. The data is alphanumeric and has a variable length up to 20 characters [1].

Example: (10) BV1234

Application Identifier (17) - Expiration date:

Application Identifier 17 indicates that the data fields contain an expiration date. The expiration date is the date that determines the limit of use of a product. For pharmaceutical products, it will indicate the possibility of an indirect health risk resulting from the ineffectiveness of the product after that date.
The structure of the date is: year, year, month, month, day, day [1].

Example: (17) 180901 – September 1, 2018
Example: (17) 190100 – January 2019 (00 indicates that it is NOT a specific day in January)

Application Identifier - 21 – serial number:

Application Identifier (21) indicates that the data fields contain a serial number. A serial number is assigned to an entity for its lifetime. When combined with the GTIN, a serial number uniquely identifies an individual item. The serial number field is alphanumeric and has a variable length up to 20 characters [1].

Example: (21) 24353638VB