

NORMATIVE INSTRUCTION – IN No. 198 OF 12 DECEMBER 2022

Establishes specific requirements for the labelling of large volume parenteral solutions, solutions for irrigation, dialysis, plasma expanders, and small-volume parenteral solutions.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 7, item III, and Article 15, items III and IV of Law no. 9,782 of 26 January 1999, and Article 187, item VI and Paragraph 1 of the Internal Regulation approved by Collegiate Board Resolution – RDC no. 585 of 10 December 2021, adopts the following Normative Instruction, as decided upon in a meeting held on 7 December 2022, and I, Director-President, determine its publication.

Section I

Objective

Article 1. This Normative Instruction establishes specific labelling requirements for large-volume parenteral solutions/suspensions (LVPS), solutions for irrigation, dialysis, plasma expanders, and small-volume parenteral solutions/suspensions (SVPS) regularized with Anvisa in addition to the rules described in Collegiate Board Resolution – RDC no. 768 of 12 December 2022, and its updates.

Section II

Large-Volume Parenteral Solutions/Suspensions (LVPS), Solutions for Irrigation, Dialysis, and Plasma Expanders

Article 2. The labels of the primary packages of LVPS, solutions for irrigation, dialysis, and plasma expanders, in addition to the information required in Collegiate Board Resolution – RDC no. 768 of 12 December 2022 and its updates, must contain:

- I – The common Brazilian name (DCB, in Portuguese) of the active pharmaceutical ingredient(s) without the degree of hydration in lowercase letters;
- II – The qualitative and quantitative composition, including the degree of hydration of the active pharmaceutical ingredient(s), expressed in percentage;
- III – The electrolyte content in mEq/L or mmol/L;
- IV – Osmolarity, when applicable;
- V – The caloric content, if any; and

VI – The degree of substitution and the molecular weight of the polymer, for plasma expanders.

Article 3. The labels of the primary packages of LVPS must follow the standardization of colors provided for in Annex I.

Paragraph 1. The colors indicated in Annex I must be used for printing at least one highlighted colored area directly on the bag. The other LVPS, not included in Annex I, may not use the colors described therein as a highlight or as the main colored element of the package.

Paragraph 2. For solutions packaged in an ampoule or plastic bottle, the colors must be printed on the label attached to the primary packaging.

Paragraph 3. If it is technically impossible to print in color directly on the bag, an over bag (intermediate wrapper) with at least one highlighted colored area must be used, as determined in Annex I.

Paragraph 4. The use of the colors indicated in Annex I on lids at the insertion sites of the equipment or medicine is optional.

Article 4. The information referring to the name of the solution and concentration must be prominently placed on the bottom or side of the bag, flask, or plastic ampoule.

Article 5. The information referring to the batch number and expiration date must be placed below the essential information or on the side of the bag or bottle, as long as its visibility is guaranteed.

Article 6. Information regarding the route of administration must be highlighted, differing from the other information on the bag or label.

Section III

Small-Volume Parenteral Solutions (SVPS)

Article 7. The labels on SVPS primary packaging must meet the requirements of Collegiate Board Resolution – RDC no. 768 of 12 December 2022 and its updates, in addition to complying with the provisions of this regulation.

Article 8. Recording information directly on ampoules, vials, syringes, or other packaging containers is not allowed.

Paragraph 1. The information on the primary packaging label must be printed on an indelible adhesive label.

Paragraph 2. For substances without a specific provision in this regulation, the printing of essential information on the label must be in the background, which allows for the letters to be printed in a contrasting manner.

Article 9. The name of the active pharmaceutical ingredients of the medicines listed in Annex II must be printed in black or, in the case of dark backgrounds, in white, thus ensuring contrast, over the color band indicated in Annex II, for the respective family.

Sole paragraph. The other wordings may be printed in the marketing authorization holder's color of choice, as long as it is on a contrasting background, in order to guarantee perfect legibility.

Article 10. For medicinal products listed in Annex III, the standardized colors for opening/breaking systems, ampoule identification rings, and text printing on adhesive labels must comply with the provisions of the Tables in Annex III.

Paragraph 1. The identification rings on the rod must have a minimum width of 0.6 (six tenths) mm.

Paragraph 2. When the medicine consists of only one active pharmaceutical ingredient, the two identification rings must be of the same color indicated for the family.

Paragraph 3. In the case of an association with a maximum of two active pharmaceutical ingredients, each identification ring must correspond to the color indicated for the respective family.

Paragraph 4. If the active pharmaceutical ingredient is an antagonist, one of the identification rings must be white and the other must be the color indicated for the family of the active pharmaceutical ingredient to be antagonized.

Article 11. SVPS packages that do not allow for identification by means of rings must be differentiated by the color criteria for printing on the label, and placement of a band with a minimum width of 3 mm (three millimeters) at the top of the label, defined in Annex III.

Article 12. The color combinations established in this regulation are for the exclusive use of the medicinal products listed in the Annexes of this Normative Instruction.

Sole paragraph. New medicinal products that may be developed, whose therapeutic activity falls within the families of Annex II, must follow the guidelines established for them regarding their identification.

Article 13. Medicinal products with different concentrations, included in the Annexes of this Normative Instruction, must present opening/rupture systems and identification rings with the colors indicated in the respective Annex.

Sole paragraph. For different concentrations of medicinal products not described in this Normative Instruction, a strategy for differentiating the concentrations must be adopted.

Article 14. The colors defined in this normative instruction may be obtained by mixing pigments from any paint manufacturer, with maximum and minimum variations.

Article 15. For parenteral solutions packaged in plastic bags, the provisions of Section II must be complied with.

Subsection I

Arrangement of Information on Primary Packaging Labels

Article 16. The labels of the SVPS primary packaging must present dimensions in such a way as to involve, at most, 3/4 (three quarters) of the total area of the container body

and the free space to allow visualization of the container content must be in its longitudinal direction and occupy the largest possible area, as shown in Figure 1 of Annex IV.

Article 17. The minimum height of the largest character of the essential information must be 2.0 mm (two millimeters).

Paragraph 1. When it is not possible to meet the criteria referred to in the caption of this article, a technical justification must be presented, and the largest possible size of characters must be used.

Paragraph 2. The minimum height of the characters of the other information must be 1 mm (one millimeter).

Article 18. The information printed on the SVPS primary packaging label must be arranged parallel to the longest axis of the container, with the left margin of the label starting as close as possible to the base and must allow the full reading of the text when the container is held by the stem or bottleneck, as shown in Figure 2 of Annex IV.

Paragraph 1. When the name of the medicine, the DCB of the active pharmaceutical ingredient, the concentration, and total volume can be printed within 180° of the circumference of the container, the printing may be done perpendicularly to its longest axis, according to Figure 3 of Annex IV.

Paragraph 2. For pre-filled syringes, the text must be oriented in the "needle - plunger" direction and in such a way as not to compromise the visualization of its graduation, according to Figure 4 of Annex V.

Article 19. Considering the transitional stage of replacement of some color standards in the PMS system (Pantone Matching System), in the event of discontinuation of the color standards defined in Annexes I, II, and III, the variations and references provided for in Annex VI must be adopted.

Article 20. This Normative Instruction shall come into force on 3 July 2023.

ANTONIO BARRA TORRES

Director-President

ANNEX I

Color standardization for LVPS

LVPS	Color	Pantone Reference
physiological solution (NaCl 0.9%)	Yellow	106C, 107C, 108C
glucose	Blue	293C, 294C, 295C
simple ringer	Orange	1505C, 151C, 152C
ringer with lactate	Brown	476C, 477C, 478C
glyco-physiological solution	Green	348C, 349C, 350C
20% mannitol	Pink	212C, 213C, 214C
sterile water	White	-
sodium bicarbonate	Red	1795 to 1805C

ANNEX II

Families of medicines used in anesthesia, intensive care, and hospital emergency with the color codes

Families of medicines used in anesthesia, intensive care, and hospital emergency, and the standardization of colors for bands and opening/breaking systems.

Table 1 – Standard colors for bands and opening/breaking systems

Therapeutic class:	Drug(s)	Band color and opening/breaking system
General anesthetics	ketamine hydrochloride (01937) etomidate (03731) methohexital (05864) propofol (07474) thiamylal (08508) thiopental sodium (08638)	Yellow 109
Anxiolytics	diazepam (02904) lorazepam (05417) midazolam (05937) oxazepam (06685)	Orange 151
Parasympathomimetic	neostigmine methyl sulfate (06288), sugammadex (09647)	Red 1795 and White (diagonal lines)
Opioid analgesics	buprenorphine (01555) fentanyl citrate (04005) sufentanil citrate (08085) alfentanil hydrochloride (00535) nalbuphine hydrochloride (06203)	Blue 286
	pethidine hydrochloride (07008) remifentanil hydrochloride (07664) tramadol (08806) morphine sulfate (06114) or hydrochloride (06095)	
Antipsychotics	chlorpromazine hydrochloride (02503) haloperidol decanoate (04591) droperidol (03246)	Salmon 156

Opioid analgesic and antipsychotic	fentanyl citrate + droperidol (association)	Blue 286 + Salmon 156
Local anesthetics	bupivacaine hydrochloride (01552) lidocaine hydrochloride (05314) prilocaine hydrochloride (07364) procaine hydrochloride (07383) ropivacaine hydrochloride (07805)	Cool Gray 7
	- in combination with epinephrine	Violet 256
	- hyperbaric anesthetics containing 7.5% glucose	Blue 285
Peripherally acting muscle relaxants	atracurium besylate (00926) cisatracurium besylate (01187) pancuronium bromide (01427) rapacuronium bromide (01442) rocuronium bromide (07774)	Red 1795
	vecuronium bromide (01456) alcuronium chloride (02359) mivacurium chloride (06027) suxamethonium chloride (08243) gallamine triethiodide (08886)	
Non-glycosidic cardiac stimulants	dobutamine hydrochloride (03164) dopamine hydrochloride (03187) etilefrine hydrochloride (03679) phenylephrine hydrochloride (03926) epinephrine (03441)	Violet 256
	metaraminol hemitartrate (05745) norepinephrine (06486) ephedrine sulfate (03311)	

Antihypertensives	clonidine (02302) diazoxide (02906) phentolamine (04015) sodium nitroprusside (06442) nitroglycerin (06440) trimethaphan camsylate (01684)	Violet 256 and White (diagonal lines)
Drugs for functional bowel disorders	glycopyrronium bromide (01408) atropine sulfate (00935)	Green 367
	atropine sulfate 0.25 mg	Blank
	atropine sulfate 0.50 mg	Black
	atropine sulfate 1.00 mg	Red 1795
Antagonists	flumazenil (04134)	Orange 151 and White (diagonal lines)
	nalorphine hydrochloride (06209)	Blue 286 and White (diagonal lines)
	naloxone hydrochloride (06211)	Blue 286 and White (diagonal lines)

Table 2 – Background colors for labels applicable to syringes containing drugs used during anesthesia.

Drug class	Pantone color	Examples of drugs
Induction agents	Process Yellow C	thiopentone, methohexital, propofol, ketamine
Benzodiazepines	Orange 151	diazepam, midazolam
Benzodiazepine Antagonists	Orange 151 with diagonal white stripes	flumazenil
Muscle relaxants	fluorescent red 811	suxamethonium _b , d-tubocurare, pancuronium, atracurium, vecuronium, rocuronium, cisatracurium.
Relaxant reversal agents	Fluorescent red 811 ^a or Warm red with white diagonal stripes	neostigmine, edrophonium, pyridostigmine
Opioids	Blue 286	morphine, fentanyl, pethidine
Opioid antagonists	Blue 286 blue with diagonal white stripes	naloxone
Vasopressors	Violet 2645	adrenaline _b , ephedrine, phenylephrine, metaraminol
Hypotensive agents	Violet 2645 with diagonal white stripes	nitroprusside, nitroglycerin, phentolamine, hydralazine

Local anesthetics	Gray 401	procaine, lidocaine. bupivacaine. ropivacaine
Anticholinergic agents	Green 367	atropine, glycopyrrolate
Major tranquilizers	Salmon 156	droperidol, metoclopramide, tropisetron
Various pharmaceutical ingredients	White	oxytocin, heparin, protamine, potassium chloride, tetrahydro aminoacridine (THA), antibiotics, nonsteroidal

^{to} In case of technical impossibility for printing, the color Pantone Fluorescent red 811 C may be replaced by Pantone Warm red C

^b All printing is in black except for suxamethonium and adrenaline which are printed against a background color as reverse plate letters within a black bar running edge-to-edge across the label.

ANNEX III

Standardization of colors for bands, opening/breaking systems, identification rings in compliance with the guidelines of this normative instruction for medicines: water for injection, aminophylline, sodium bicarbonate, potassium chloride, anhydrous glucose, calcium gluconate, and magnesium sulfate heptahydrate.

Table 3 – Standard colors for text printing, opening/breaking system and ampoule identification ring.

Active Pharmaceutical Ingredient	Concentration	Label background color and identification ring	Color of the opening/breaking system against the concentration of the product
water for injection	-	White	White
aminophylline	24 mg/mL	Green 357 C (variation: 356 C)	Green 357 C (variation: 356 C)
sodium bicarbonate	3%	Red 1795 C (variation: 1805 C)	Yellow 109 C (variation: 110 C)
	8.4 %		Blue 285 C (variation: 286 C)
	10 %		Red 1795 C (variation: 1805 C)
potassium chloride*	10.0%	Black	White
	15.0%		Yellow 109 C (variation: 110 C)
	19.1%		Brown 4695 C (variation: 4705 C)
	20.0%		Orange 1595 C (variation: 1585 C)
sodium chloride	0.9%	Yellow 109 C (variation: 110 C)	White
	10.0%		Blue 285 C (variation: 286 C)
	20.0%		Red 1795 C (variation: 1805 C)
potassium phosphate	2 mEq	Black	Black
glucose anhydrous	5%	Blue 285 C (variation: 286 C)	Blue 285 C (variation: 286 C)
	10%		White
	25%		Green 357 C (variation: 356 C)
	50%		Yellow 109 C (variation: 110 C)

calcium gluconate	10%	Orange 1595 C (variation: 1585 C)	Orange 1595 C (variation: 1585 C)
magnesium sulfate heptahydrate	10%	Brown 4695 C (variation: 4705 C)	Blue 285 C (variation: 286 C)
	50%		Yellow 109 C (variation: 110 C)
	1 mEq/mL		Green 357 C (variation: 356 C)

* Due to the potential hazard of the product, a red band of at least 3-mm must be added.

ANNEX IV

Figure 1 – Ampoule with label representation

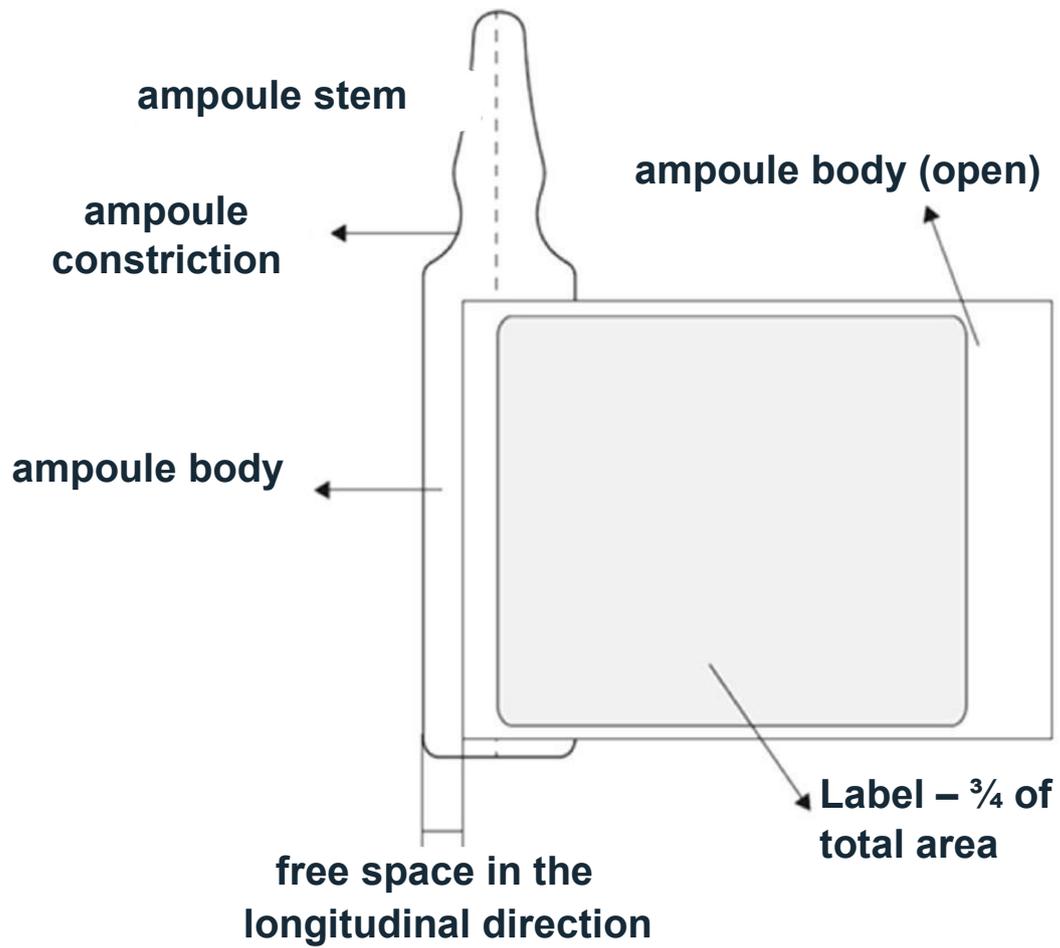


Figure 2 – Printed parallel to the longest axis of the container

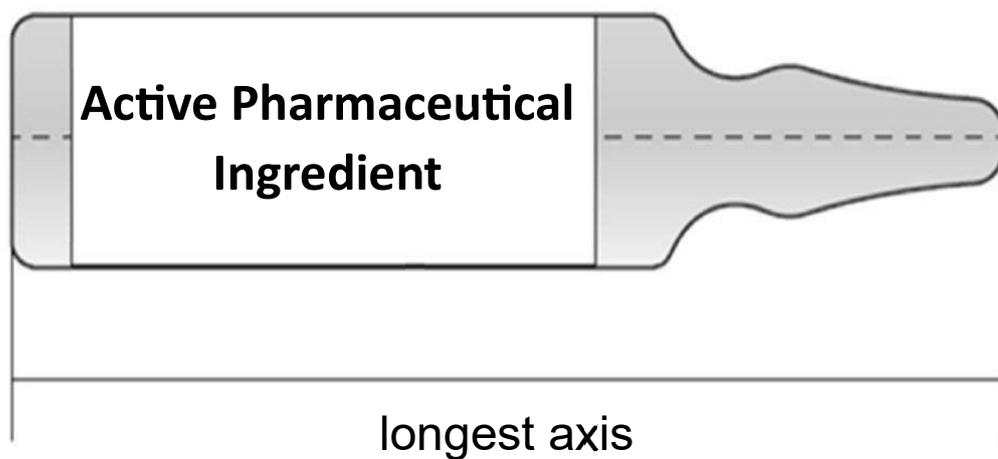
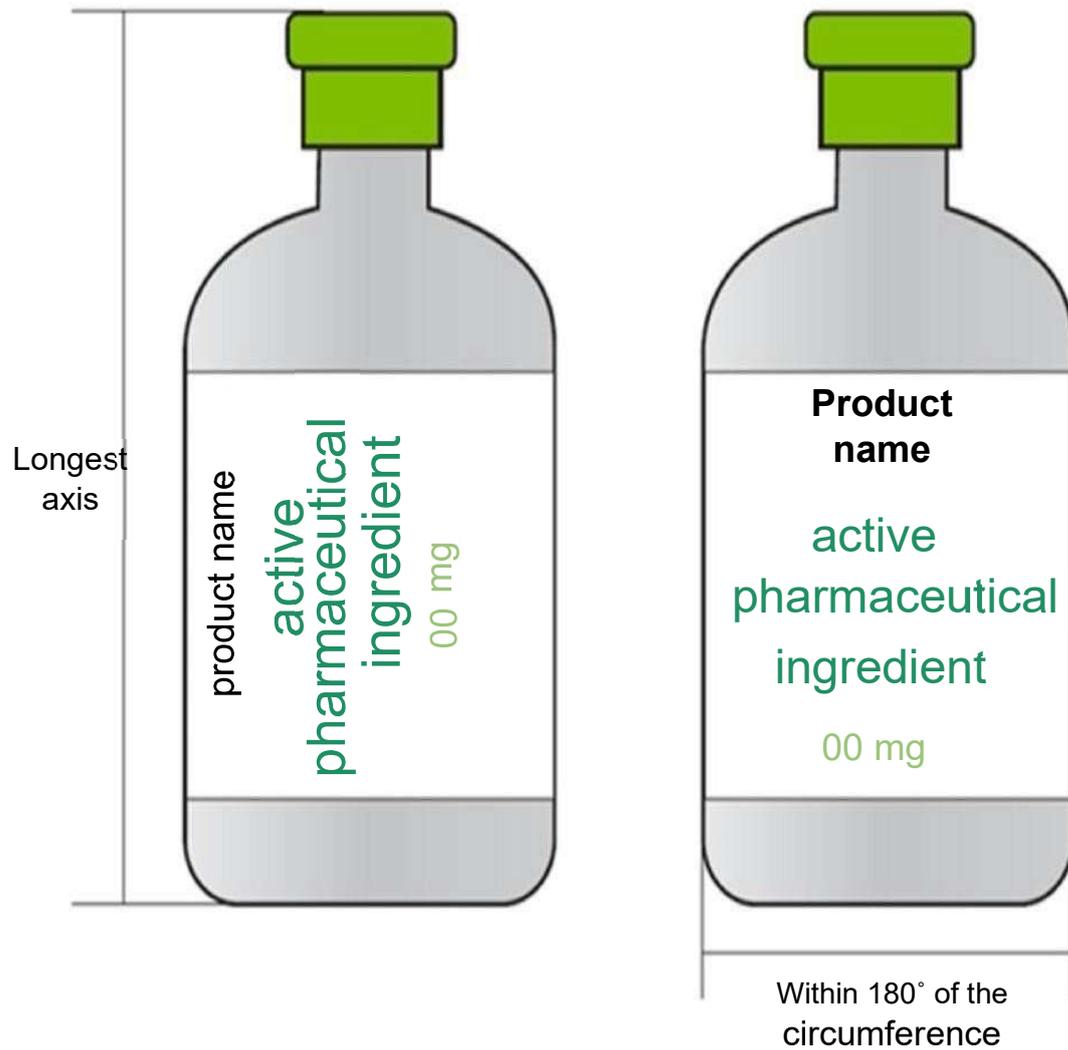
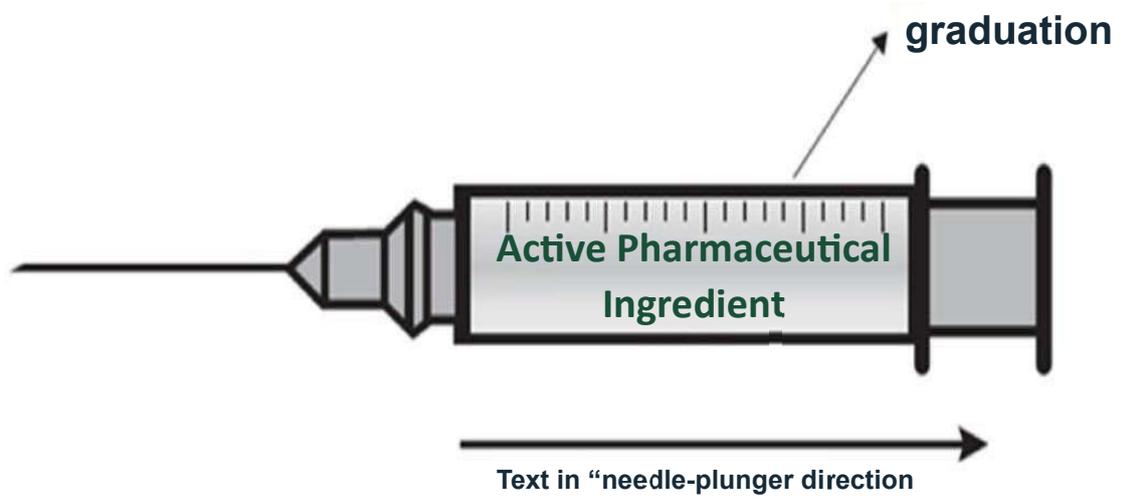


Figure 3 – Printed parallel and perpendicular to the longest axis of the container



ANNEX V

Figure 4 – Text starting from the end of the needle



ANNEX VI

Table 4 – Variations and references allowed in case of unavailability of PMS system standards

Colors	Current reference	Current variation	New reference	New variation
White				
Yellow	110	109	586	587
Blue	286	285	285	284
Light blue	284	283	278	277
Gray	Cool gray 7	Cool gray 6	Cool gray 7	Cool gray 6
Orange	1595	1585	130	129
Brown	4695	4705	7595	7594
Black	Process Black	Process Black	Black	Black
Salmon	156	155	714	713
Green	357	356	348	347
Red	1805	1795	7621	7620
Violet	257	256	257	256