Imagine the possibilities

POSTMIDYEAR ASHP

14 FEBRUARY 2024

Organiza:

sefh
Sociedad Española de Farmacia Hospitalaria

Con la colaboración de:

AMGEN®

Seguridad y Elaboración

Francisco Sierra. Jefe de Servicio HUTorrecárdenas, Almería

Organiza:

sefh
Sociedad Española
de Farmacia Hospitalaria

Con la colaboración de:

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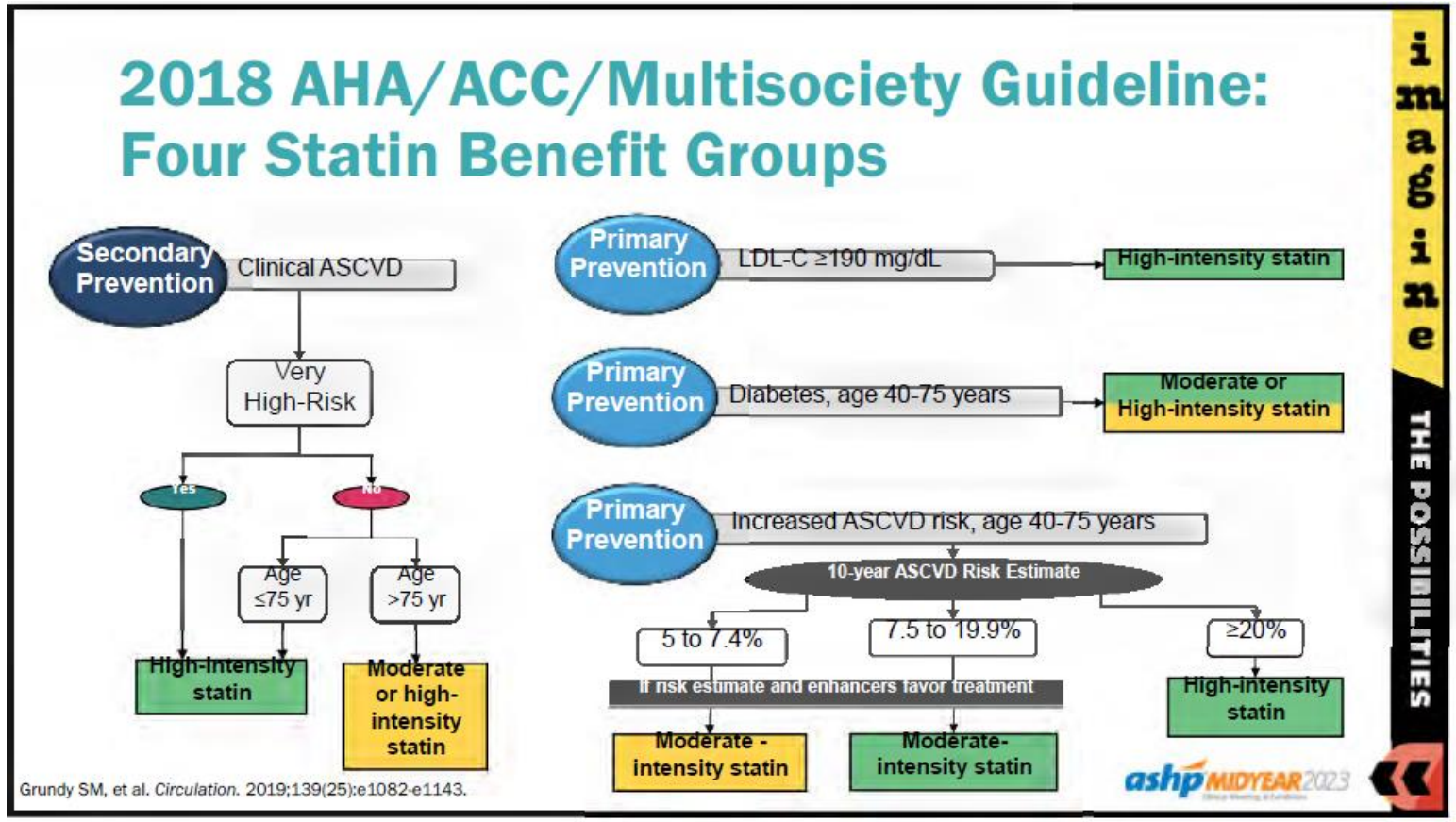
Esto (sino me enrollo) y lo que me dejo en el tintero

- Seguridad CV : Nocebo en estatinas
- Nueva USP 797 : “Noviembre 23”
- Nuevas (y no tan nuevas) recomendaciones ISMP
- y ¿Nueva NHIOS?
- Mensajes para “hacer en casa”

Statin Intolerance, Statin Defiance, Nocebo Effect ... Does it Really Matter?

- ¿Porque me llamó la atención? ¿Se acabó el estatinocentrismo?
- La realidad es que al haber más alternativas,,,, se pueden tomar diferentes decisiones y haber mayor variabilidad clínica



EXPERT CONSENSUS DECISION PATHWAY

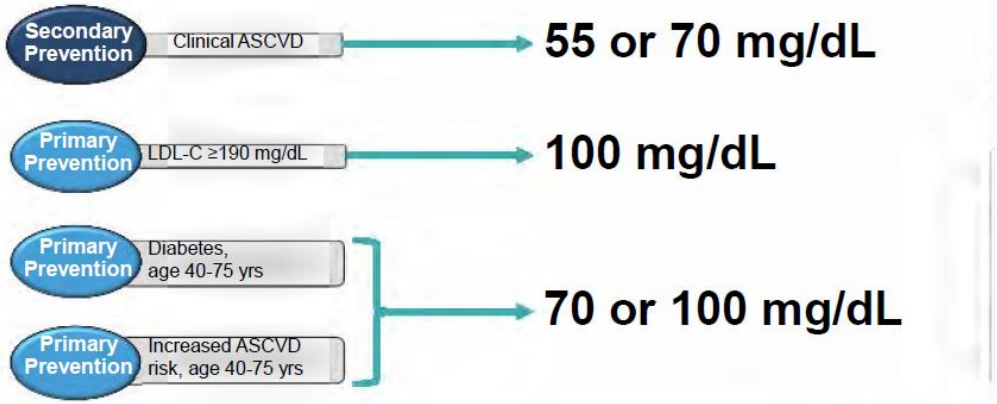
2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk

A Report of the American College of Cardiology Solution Set Oversight Committee

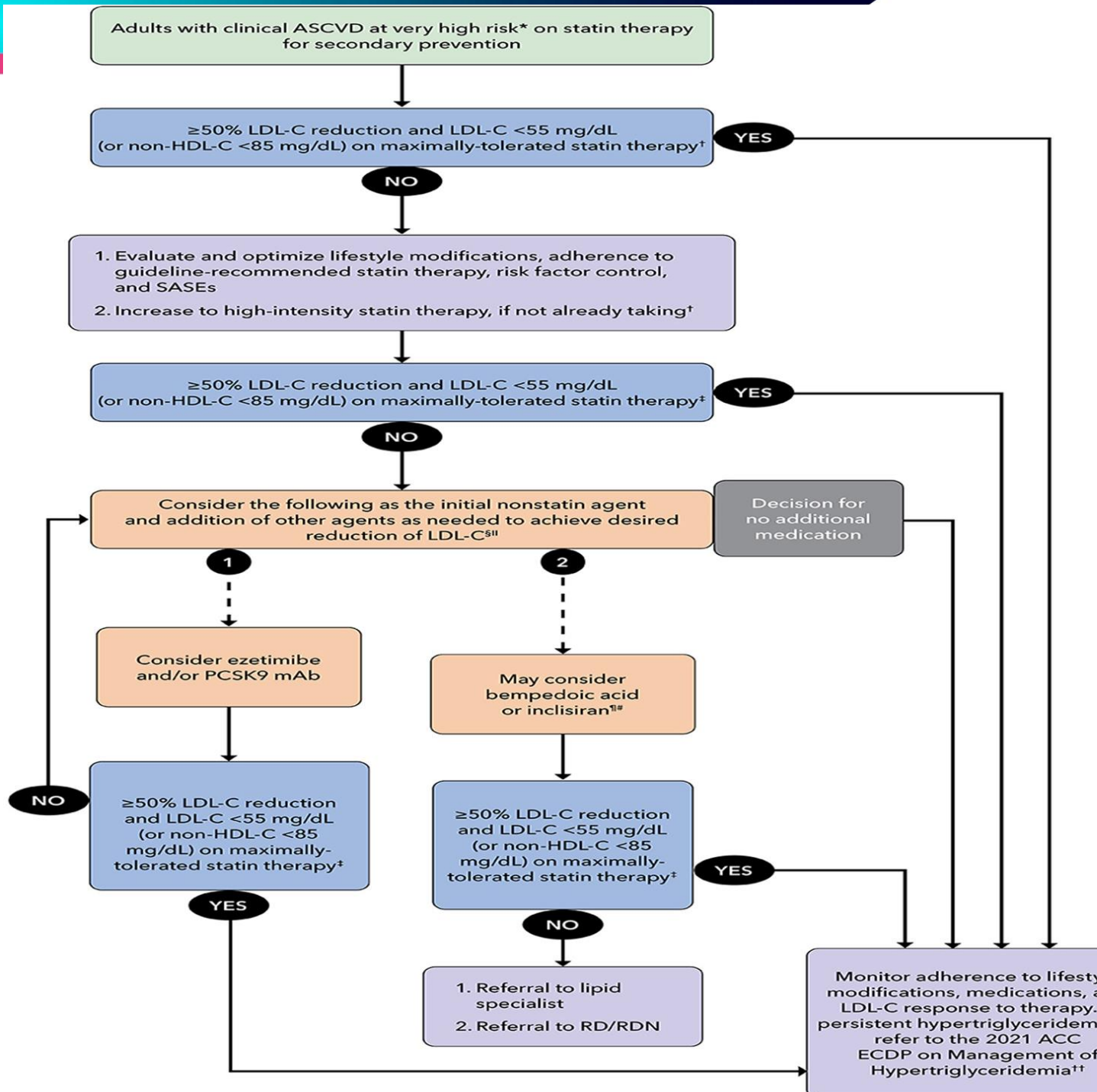
Endorsed by the National Lipid Association

- Consistent with expert guidance provided in the 2017 ACC nonstatin ECDP, [6] the 2018 AHA/ACC/multisociety cholesterol guideline recommends use of an LDL-C threshold of ≥70 mg/dL (1.8 mmol/L) to consider the addition of nonstatin therapy to maximally tolerated statin therapy in patients with ASCVD.[7]

2022 ACC ECDP: LDL-C Thresholds



Joyd-Jones DM, et al. *J Am Coll Cardiol*. 2022 Oct, 80 (14) 1366–1418



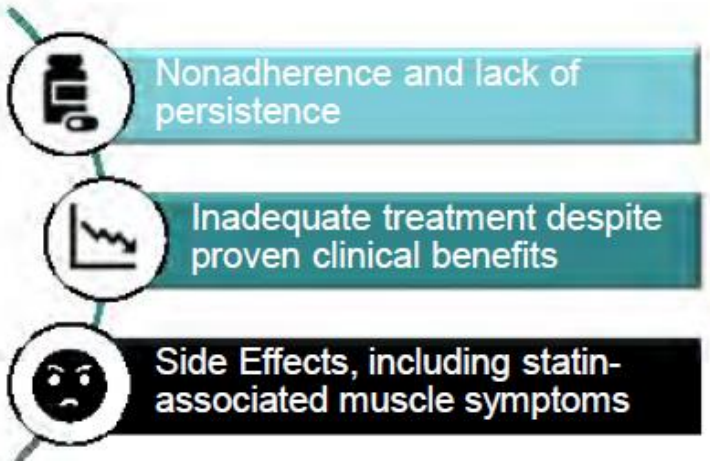
Statin-Associated Muscle Symptoms (SAMS)

Type	Frequency
Myalgia Creatine kinase (CK) is normal Unexplained muscle discomfort: • "flu-like" including Muscle aches, soreness, stiffness, tenderness, cramps with or shortly after exercise	• Infrequent (1%-5%) in clinical trials • Frequent (5%-10%) in observational studies and clinical setting
Myositis/Myopathy CK >3 x the upper limit of normal (ULN) with concerning symptoms/objective weakness	Rare
Rhabdomyolysis CK >10 x ULN with renal injury (acute serum creatinine increase ≥0.5 mg/dL)	Rare

Statin Therapy

High-intensity	Moderate-intensity
Daily dose that provides ≥50% LDL-C lowering	Daily dose that provides 30-49% LDL-C lowering
• Atorvastatin 40-80 mg • Rosuvastatin 20-40 mg	• Atorvastatin 10-20 mg • Rosuvastatin 5-10 mg • Simvastatin 20-40 mg • Pravastatin 40-80 mg • Lovastatin 40-80 mg • Fluvastatin 80 mg • Pitavastatin 1-4 mg

• Limitations



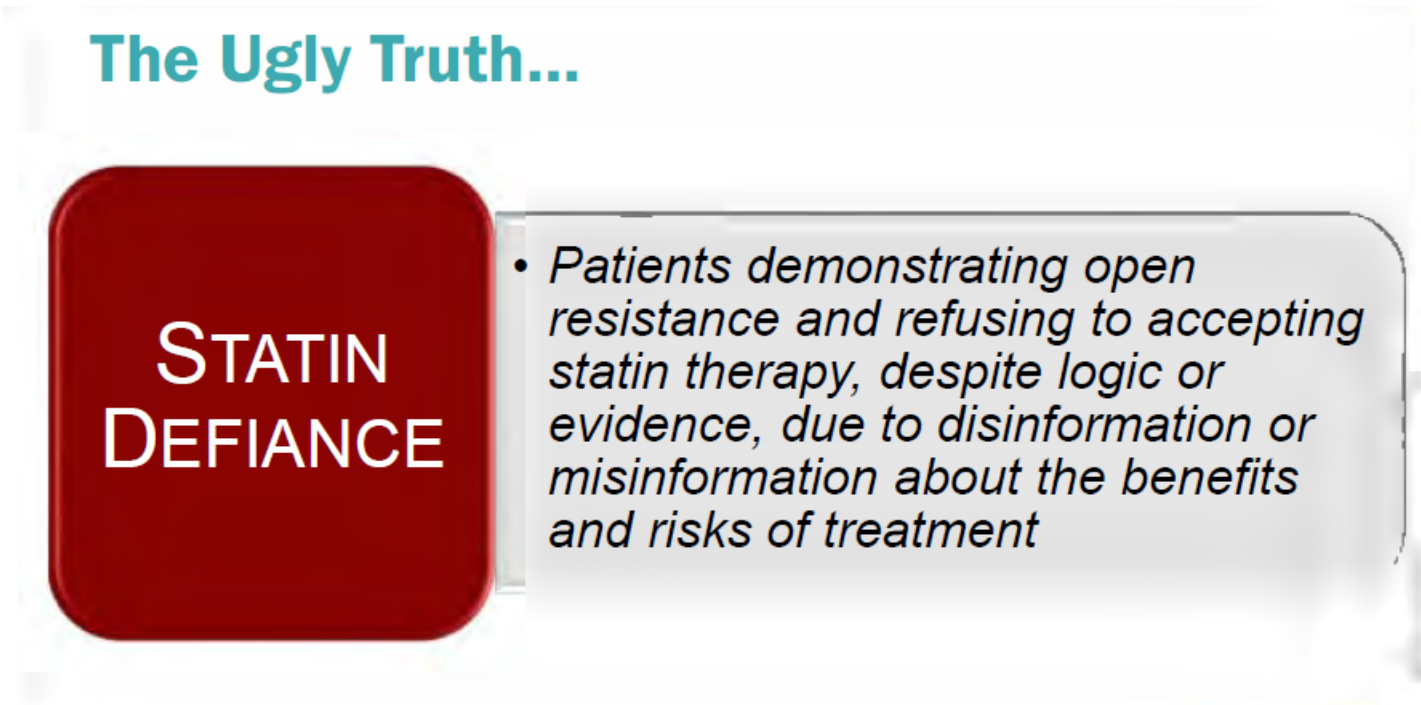
CORRESPONDENCE

N-of-1 Trial of a Statin, Placebo, or No Treatment to Assess Side Effects

November 26, 2020
N Engl J Med 2020; 383:2182-2184
DOI: 10.1056/NEJMc2031173

TO THE EDITOR:

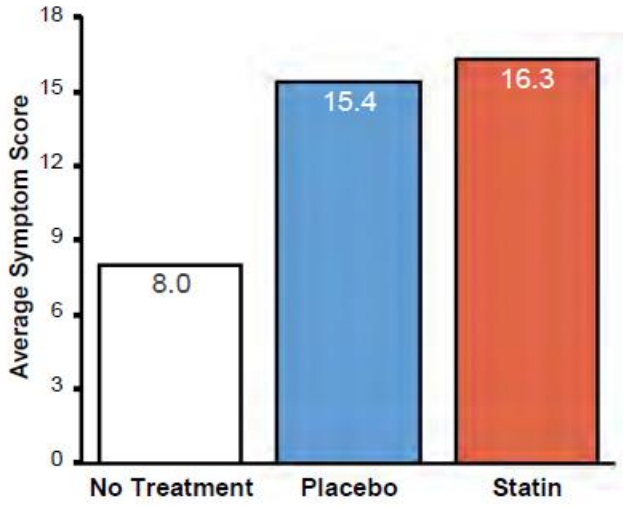
Statins are often discontinued because of side effects,[1,2] even though some blinded trials have not shown an excess of symptoms with statins as compared with placebo.[3,4] Patients who had previously



SAMSON: N-of-1 Trial

- 60 patients who had abandoned statin therapy with no intention of restarting because of intolerable symptoms arising within 2 weeks
- Multiple-crossover, 3-arm, double-blind, placebo-controlled design for 12-months:
  - four atorvastatin 20 mg bottles
  - four placebo bottles
  - four empty bottles (NIL)
- Each bottle contained a 30-day supply; random sequence
- Patients reported symptom intensity daily
  - 0 (no symptoms) to 100 (worst imaginable)

Baseline Characteristics	
Mean Age (years)	65.5
Male:Female (n)	35:25
Ethnicity (n): • White • Black/Asian/Mixed	 54 1/3/2
Number of statins prior: • 1 • 2 • 3 • 4 • 5	 13 24 11 7 5
Mean prior statin duration (years)	2.84



P<0.001 no treatment vs placebo and statin
P=0.39 placebo vs statin

- Más del 90% de los síntomas provocados por las estatinas, se provocaban también con el placebo
- La mitad de pacientes “Intolerantes” volvieron a tomarlas

- Symptom patterns seen:
  - “Ever Present”
    - Patients who experienced intense symptoms throughout all months
  - “Successful Re-challenge”
    - Patients experiencing virtually no side effects
  - “Nocebo Effect”
    - Patients experiencing similar symptoms from statin vs placebo, but not with NIL

TOOLS FOR PRACTICE

PEER

Wouldn't Bet On it: What is the risk of muscle symptoms on statins?

CLINICAL QUESTION

What are the effects of statins on muscles?

BOTTOM LINE

Statins increase the risk of muscle symptoms (includes pain, cramps, and weakness) in their first year of use, from 14% (placebo) to 14.8%, but are similar to placebo after 1 year. When patients report muscle symptoms, only 1 in 15 is due to the statin. Statins may increase muscle symptoms with creatine kinase rise 10x normal for 1 in ~3000 patients over placebo.

EVIDENCE

- 7 systematic reviews [11-135 randomized controlled trials (RCTs); 18,192-192,977 patients] from the last 5 years.[1-7] Focusing on the most recent (23 RCTs; 154,664 patients x4.3 years).[1] Results statistically significant unless indicated.
  - Any muscle symptoms, statin versus placebo,
    - Anytime: 27.1% versus 26.6% (placebo).[1]
      - Within 1st year: 14.0% versus 14.8%, number needed to harm=125.
      - After 1st year: 14.8% versus 15.0% (not statistically different).
    - Other systematic reviews[2-7] similar but not statistically different for myalgia,[5] ≥65 age subgroup,[4] or intensity subgroups versus placebo.[2]
    - No difference by statin type,[3] lipophilic/hydrophilic statin,[6] or age groups.[1,5,6]

European Heart Journal

Volume 43, Issue 34
7 September 2022

Article Contents

JOURNAL ARTICLE

Prevalence of statin intolerance: a meta-analysi

Ibadete Bytyçi, Peter E Penson, Dimitri P Mikhailidis, Nathan D Wong, Adrian V Hernandez, Amirhossein Sahebkar, Paul D Thompson, Mohsen Mazidi, Jacek Rysz, Daniel Pella ... Show more
Author Notes

European Heart Journal, Volume 43, Issue 34, 7 September 2022, Pages 3213–3223
https://doi.org/10.1093/eurheartj/ehac015
Published: 16 February 2022 **Article history** ▾

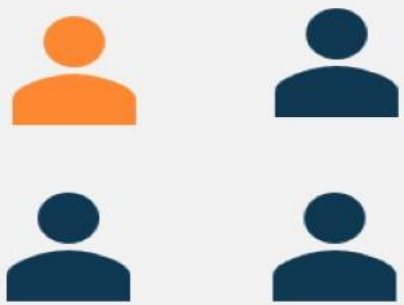
Conclusion

Based on the present analysis of >4 million patients, the prevalence of SI is low when diagnosed according to international definitions. These results support the concept that the prevalence of complete SI might often be overestimated and highlight the need for the careful assessment of patients with potential symptoms related to SI.

prevalence of complete SI is often overestimated and highlights the need for a very careful assessment of patients with SI, to decrease the risk of unnecessary statin discontinuation, and suboptimal lipid-lowering therapy. Clinicians should use these results to encourage adherence to statin therapy in their patients.

Achievement of Guideline-Derived LDL-C Targets in Patients With CAD

ACC/AHA Guideline Target: ≤ 70 mg/dL



Almost 3 in 4 participants did not meet ACC/AHA guideline target

ESC Guideline Target: ≤ 55 mg/dL

9 in 10 did not meet ESC guideline target

- **73.5%** (95% CI, 68.2%, 78.8%) of participants had an LDL-C level ≥ 70 mg/dL
- **88.1%** (95% CI, 83.6%, 92.6%) had an LDL-C level ≥ 55 mg/dL

ACC, American College of Cardiology; AHA, American Heart Association; ESC, European Society of Cardiology.
Aggarwal R, et al. JAMA. 2023;330:80-82.

Low Rate of LLT Use in Patients With CAD

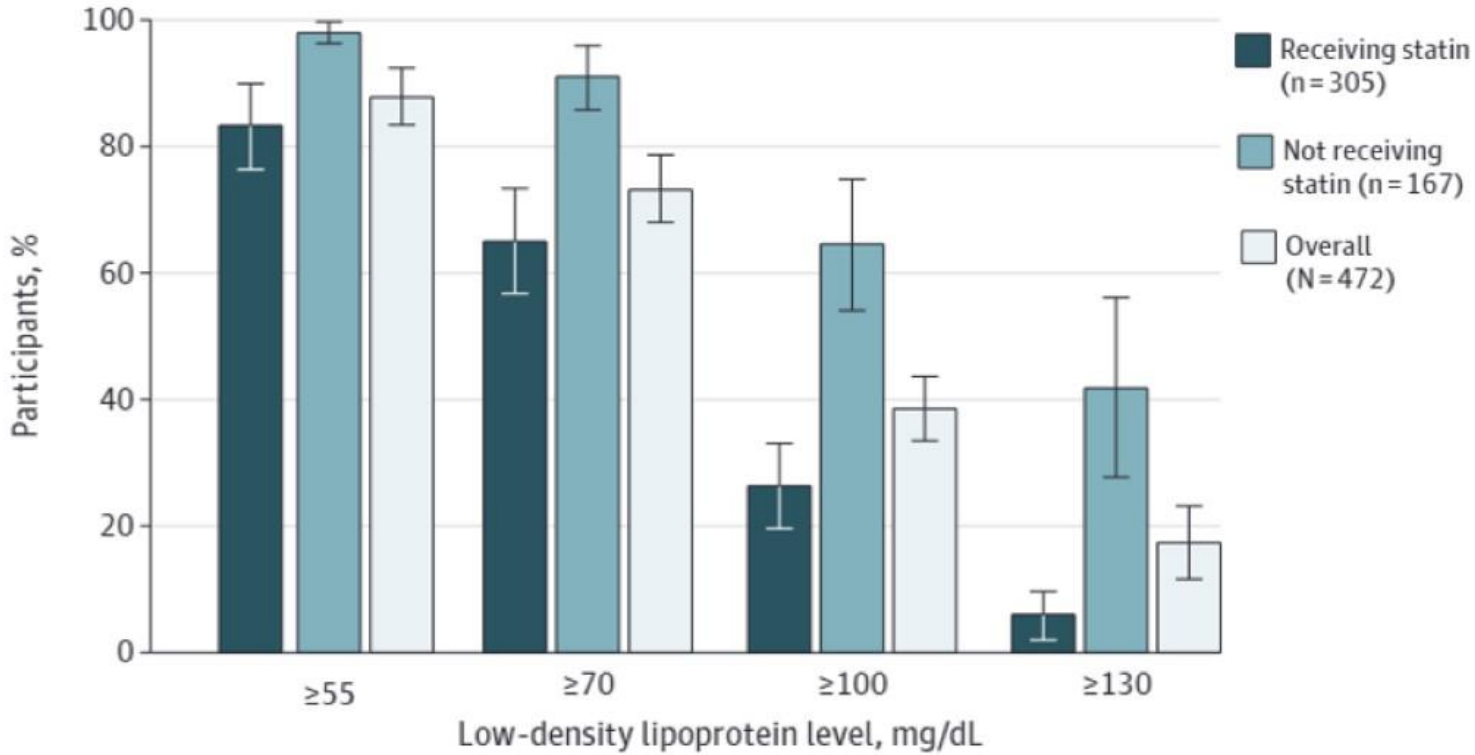
Data From NHANES
(January 2015-March 2020)

People aged ≥ 20 y with CAD (defined as self-report of previous coronary heart disease, angina, or "heart attack")

Among Adults With CAD

- 67.9% on statin therapy
- 6.4% on ezetimibe

LDL-C Levels Among Adults With CAD in the US



CAD, coronary artery disease; NHANES, National Health and Nutrition Examination Survey.
Aggarwal R, et al. JAMA. 2023;330:80-82.

Table 1. Baseline Characteristics According to Achieved LDL-C Level in FOURIER-OLE

Characteristics	Achieved LDL-C level, mg/dL					
	<20 (n=1604 [24%])	20–<40 (n=2627 [40%])	40–<55 (n=1031 [16%])	55–<70 (n=486 [7%])	≥70 (n=811 [12%])	*P* trend
Achieved LDL-C level, mg/dL	14.0 (10.0, 17.0)	28.5 (24.0, 33.5)	45.5 (42.5, 49.5)	61.5 (58.0, 65.0)	92.5 (79.5, 117.5)	–
Demographic characteristics						
Age, y	63.5±8.0	63.0±8.5	61.4±8.9	61.4±8.6	60.2±8.9	<0.0001
Male	1375 (85.7)	2079 (79.1)	761 (73.8)	320 (65.8)	501 (61.8)	<0.0001
BMI, kg/m^2	29.3±4.5	29.8±4.9	30.3±5.4	30.6±5.9	30.5±6.4	<0.0001
White	1575 (98.2)	2538 (96.6)	980 (95.1)	441 (90.7)	728 (89.8)	<0.0001

Por otra parte, en relación con su consulta sobre variabilidad interindividual de los pacientes en tratamiento con evolocumab, indicarle que el estudio de asociación entre los niveles alcanzados de C-LDL y los resultados cardiovasculares, no se menciona la variabilidad interindividual, sin embargo, adjunto le enviamos un análisis del estudio FOURIER donde se menciona este tema [Qamar, et al. JAMA Cardiology. 2019]. En este estudio, evolocumab redujo los niveles de C-LDL en un 50% o más, en el 90,5% de los pacientes, y en un 30% o más, en el 99,8% de los pacientes.

Medications at baseline						
High-intensity statin*	1208 (75.3)	2009 (76.5)	796 (77.2)	369 (75.9)	654 (80.6)	0.0092
Ezetimibe	61 (3.8)	138 (5.3)	70 (6.8)	39 (8.0)	71 (8.8)	<0.0001
Laboratory data						
Baseline LDL-C, mg/dL	83.0 (75.0, 95.0)	91.0 (80.0, 104.5)	96.0 (81.5, 111.5)	101.0 (86.5, 120.5)	108.0 (87.0, 137.0)	–
Lipoprotein(a) at 12 weeks, nmol/L	8.0 (3.0, 40.0)	24.5 (6.0, 130.0)	41.0 (7.0, 156.0)	44.0 (9.0, 152.0)	40.0 (9.0, 146.0)	<0.0001
HbA1c, %	6.1±1.0	6.1±1.1	6.1±1.1	6.3±1.4	6.3±1.4	<0.0001

Values are median (interquartile range), mean±SD, or n (%). BMI indicates body mass index; FOURIER-OLE, Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk–Open-Label Extension; LDL-C, low-density lipoprotein cholesterol; and TRS 2°P, TIMI Risk Score for Secondary Prevention.

Statins for preventing cardiovascular disease

There is a [NICE patient decision aid to support discussions about statin therapy to reduce the risk of heart disease and stroke]

Should I take a statin?

This decision aid can help you if you are thinking about taking a statin. It is for people who do not already have heart disease and have not had a stroke. You can use it to help you to talk about your options with your healthcare professional (such as your doctor, pharmacist or nurse).

There are advantages and disadvantages to taking a statin, which this decision aid explains. **It is important that you make a decision that is right for you.**

You might want to think about:

- What are heart disease and stroke?
- What is my risk of heart disease or stroke?
- What can I do to reduce my risk?
- How could a statin help?
- What does taking a statin involve?
- How much will a statin reduce my risk?
- What are the possible side effects of statins?

Your healthcare professional can help with questions you may have.

Effect of a statin on your risk of heart disease or stroke over the next 10 years

If your QRISK score is 8% over the next 10 years

On average, for every 100 people with this risk score who do not take a statin, over 10 years 8 people will get heart disease or have a stroke and 92 will not.

If 100 people take a statin, over 10 years on average:

- about 92 people will not get heart disease or have a stroke, but would not even if they had not taken a statin
- about 3 people will not get heart disease or have a stroke because they take a statin
- about 5 people will get heart disease or have a stroke even though they take a statin

If your QRISK score is 25% over the next 10 years

On average, for every 100 people with this risk score who do not take a statin, over 10 years 25 people will get heart disease or have a stroke and 75 will not.

If 100 people take a statin, over 10 years on average:

- about 75 people will not get heart disease or have a stroke, but would not even if they had not taken a statin
- about 9 people will not get heart disease or have a stroke because they take a statin
- about 16 people will get heart disease or have a stroke even though they take a statin

We cannot say for sure what will happen to any specific person

Mensajes para casa

- No me gustaría tener LDL alto
- Y si lo tuviera, rogaría por no ser intolerante a las estatinas,,,PERO ES DIFÍCIL SERLO REALMENTE
- Los datos sugieren que la gran mayoría de los efectos adversos se deben al efecto nocebo (estrategias para evitarlo)
- MISIÓN NUESTRA: Mejorar la adherencia

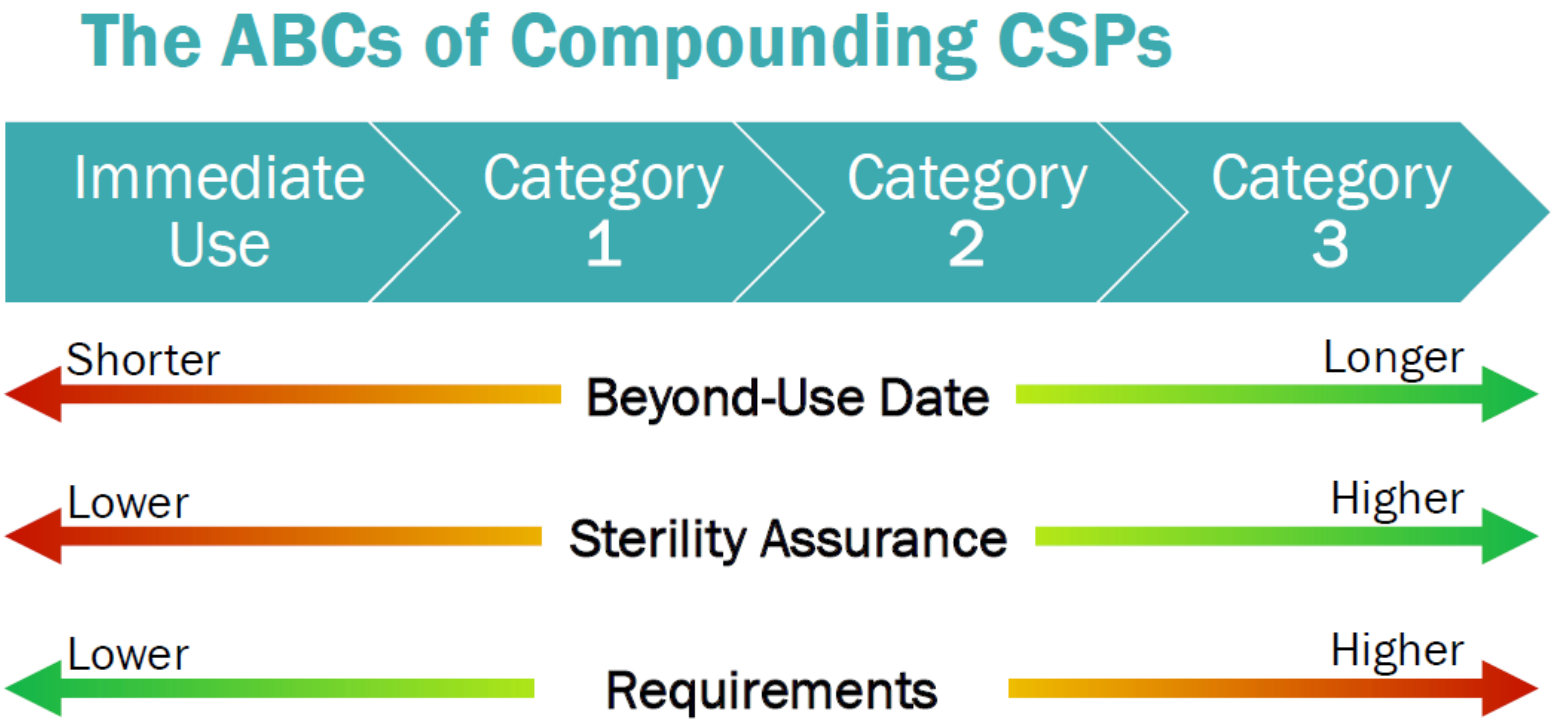
  REFORZAR en la visita a nuestras consultas: Gráficos

  Comprobar Recogida en oficinas de farmacia: Sorpresas

USP 797 :Nov 2023

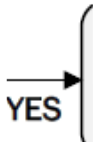
Compounding ABCs: Following Category 1, 2, & 3

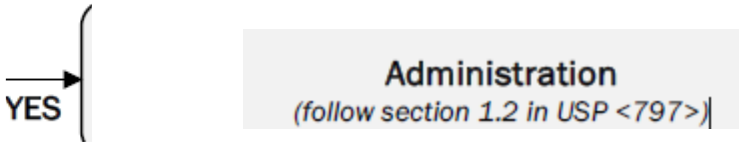
- CSP: Compounded Sterile Preparation
- Se renombran las categorías de bajo riesgo, medio y alto a categoría 1, categoría 2 y categoría 3
- Distinguen la condiciones bajo la que se hace el CSP y el tiempo en el que se pueden usar, con una intención más “neutra”



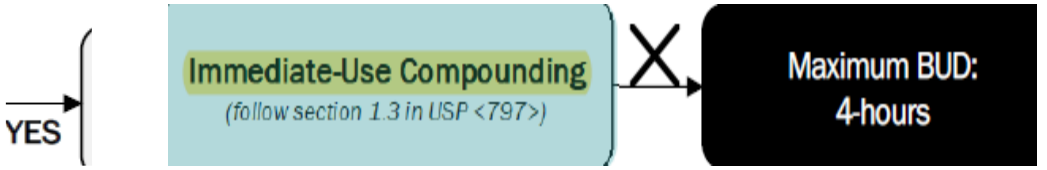
¿Cuándo se aplica?

- Will the sterile product or preparation be directly applied to an individual patient by injecting, infusing, or otherwise providing it in its final form?”



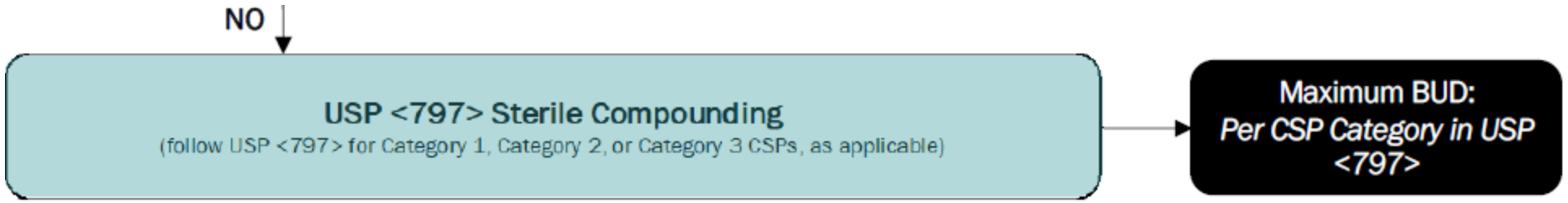


- Is the compounding activity occurring outside of an ISO Class 5 Primary Engineering Control?



¿Cuándo aplica?

- Does the activity include preparing a conventionally manufactured sterile product in accordance with the directions in the manufacturer's approved labeling for a single patient
- Does the preparation exactly follow a USP Compounded Monograph, including the specific tests and additional requirements?



USP Chapter <797>
Immediate Use CSPs

- For direct and immediate

administration

- ‘Immediate’ defined as administration

beginning *within 4 hours*

Immediate-Use: Personnel Requirements

Training	Process	Environment	Garb	Documentation
Preparer trained & demonstrates competency in aseptic technique	Minimize potential for contact with nonsterile surfaces or mix-ups	No requirements (based on standard operating procedures [SOPs])	No requirements (based on SOPs)	Must be created *if preparing for more than one patient*

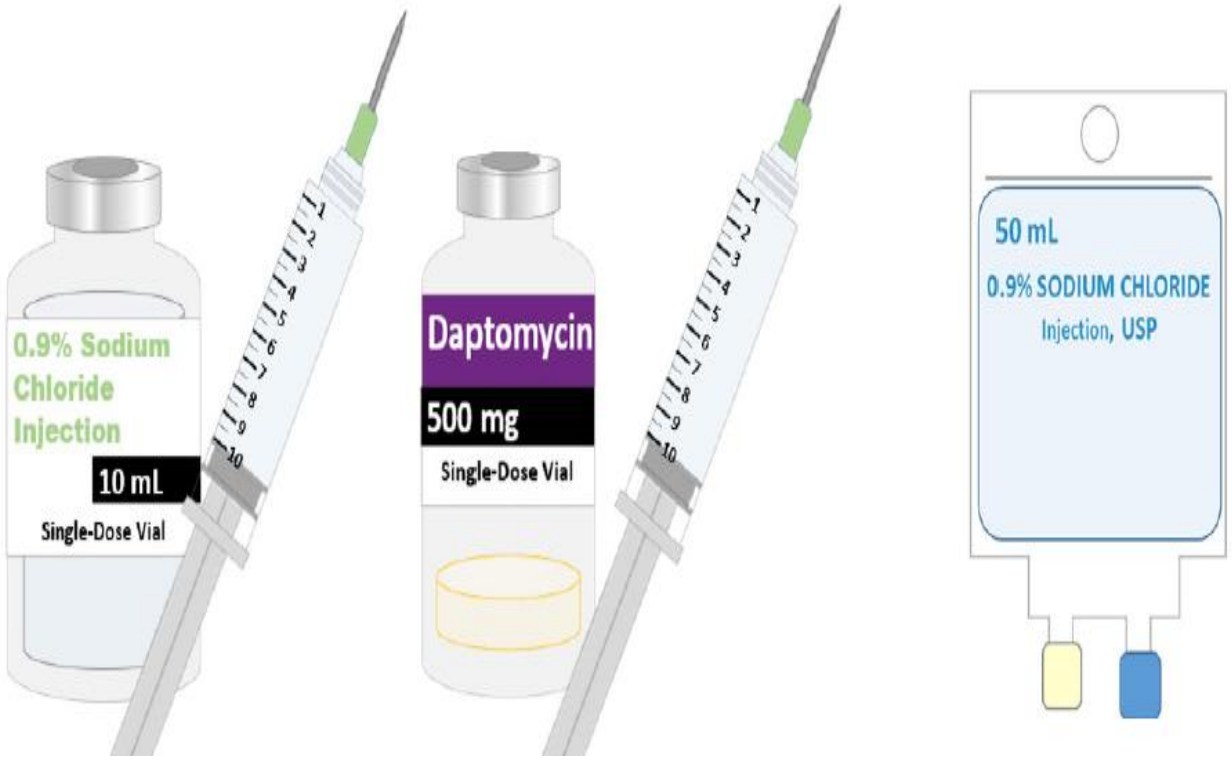
Immediate-Use: Preparation Requirements

Ingredients	Patient	Evidence	BUD	Labeling
Not more than **3** <u>different</u> **sterile** products (all must be sterile)	Single-dose containers can only be used for a single patient; *waste remnants*	Physically and chemically compatible drugs	≤ 4 hours *(does not require special storage conditions)*	Labeling if preparer not administering/ witnessing (names/amounts of all active ingredients, preparer, BUD)

Note: Hazardous Drugs must comply with USP <800>

¿Debe cumplir con la USP 97 Inmediate use?

- Daptomicina 500 mg disuelto con un vial de cloruro sódico y traspasado a una bolsa de suero estéril en una en planta



3 componentes: vial de suero, bolsa de suero y daptomicina: 3 diferentes:, agujas y jeringas no son drogas

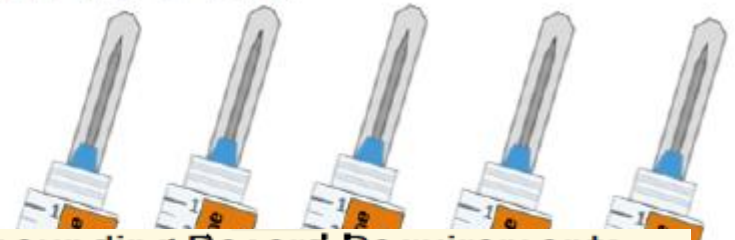
¿Y esto?

- Traspasar 3 ampollas de bicarbonato 1M a una bolsa de Glucosa al 5%

Número de transferencias: NO AFECTA: Solo hay 2 productos estériles distintos

ahora, que la USP797 lo permita, no significa que debas, o sea, piensa si puedes hacerlo: tu juicio prevalece. La USP SON MINIMOS

Does this preparation comply with immediate-use CSP requirements? (Yes/No)



Compounding Record Requirements

- Name, strength or activity, and dosage form of CSP
- Date/time of preparation
- Assigned internal ID #
- Preparer/verifier identification
- Name of each component
- Vendor, Lot #, expiration date for each ingredient
- Weight/volume of each component
- Total quantity compounded
- Final yield
- Assigned BUD and storage requirements
- Results of quality control procedures
- If applicable: master formulation record reference, calculations

LOTES:
a) múltiples dosis para un único paciente; mismos requerimientos
b) Múltiples dosis para VARIOS pacientes: HORRIBLE
Los ingredientes etiquetados como multidosis
Debes crear un registro de preparación

yes: si cumple porque es el minimos, para multiples clíncias si nacceso a farmacia: es el

Category 1 CSP s

Deben realizar en un (PEC) ISO 5.

• El PEC (primary engineering control) puede colocarse en un SAC (área de elaboración separada no clasificada) o en una sala limpia

• BUD determinada por las condiciones de almacenamiento

Temperatura ambiente controlada (20-25°C): BUD < 12 horas

Frigorífico (2-8°C): BUD < 24 horas

Categoría 2 CSPs

Nuestro equivalente: UNE 171340:2020

Validación y cualificación de salas de ambiente controlado en hospitales

Facilities and Engineering Controls

- ISO Classification
  - PEC: classified ISO 5 or better
  - Buffer room: classified ISO 7 or better
  - Anteroom: classified ISO 8 or better

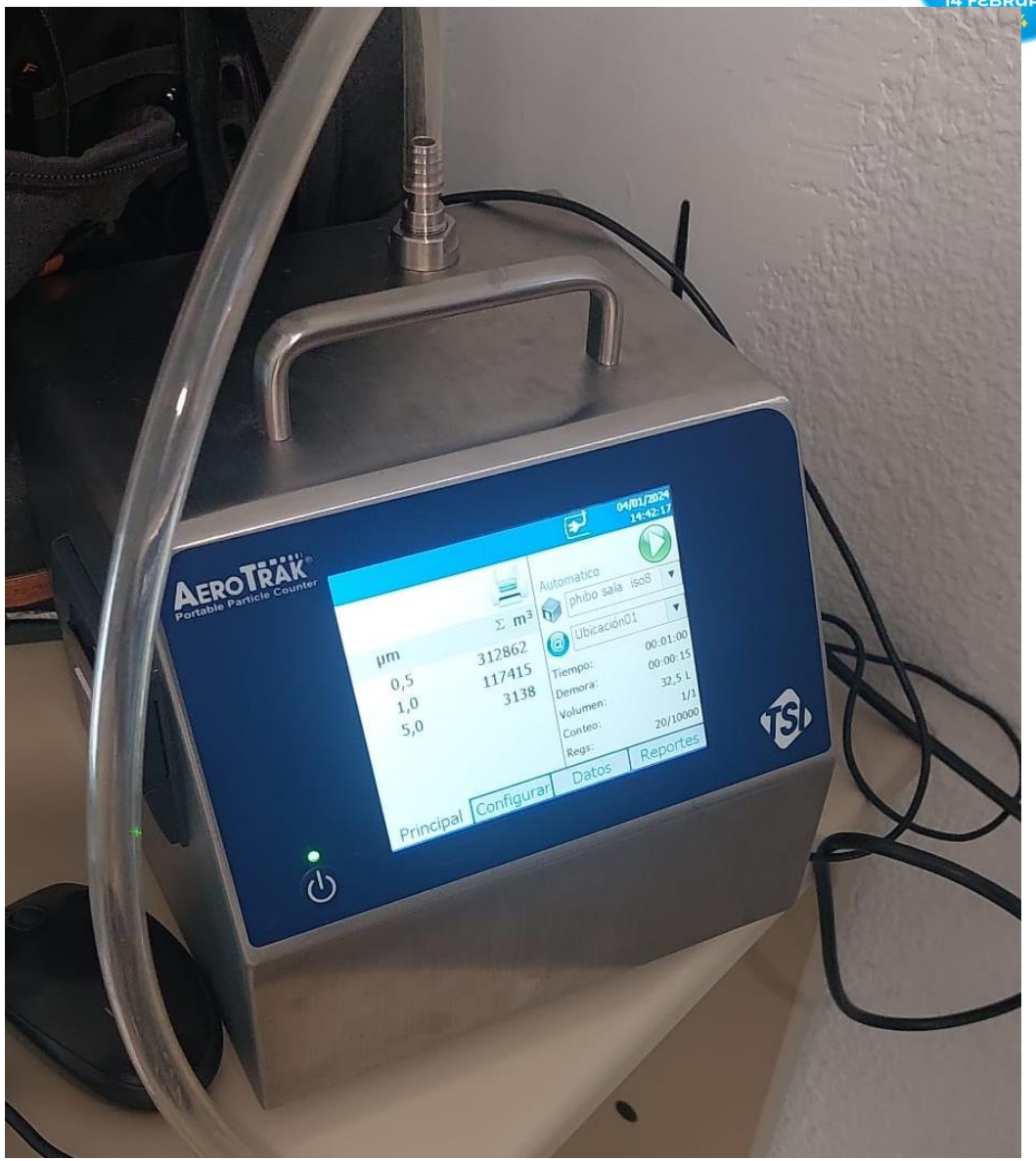
Mides

- Además de partículas:
- Caudales y renovaciones por hora
- Presiones diferenciales
- Integridad de filtros HEPA

En la siguiente tabla se resumen los criterios de evaluación generales utilizados para sopesar los valores obtenidos en las mediciones de cualificación de una sala tipo en modo operacional, según viene descrito en la tabla 3 de la Norma UNE 171340:2020

NIVEL DE RIESGO	VALORES DE PARÁMETROS AMBIENTALES POR DEFECTO						
	Tª	HR(%)	Renovaciones /hora	Clase sala	Sobre/Depresión (Pa)	Aerobios Mesófilos (ufc/m^3)	Mohos y Levaduras (ufc/m^3)
5 MUY ALTO	20-26 (1)	40-60	20	ISO 5	20 Pa	<10	Ausencia
4 ALTO	20-26 (1)	40-60	20	ISO 6	15 Pa	<10	Ausencia
3 MEDIO	20-26 (1)	40-60	15	ISO 7	10 Pa	<100	Ausencia
2 MODERADO	20-26 (1)	40-60	10	ISO 7	6 Pa	<100	<10 / Ausencia hongos patógenos (2)
1 LIGERO	20-26 (1)	40-60	5	ISO 8	2,5 Pa	<200	<25 / Ausencia hongos patógenos (2)


14:42:17
Automatico
phibo sala iso8
Σ m³
µm
312862
0,5
117415
1,0
3138
5,0
Ubicación01
Tiempo:
00:01:00
Demora:
00:00:15
Volumen:
32,5 L
Conteo:
1/1
Regs:
20/10000
Configurar
Datos
Reportes


AEROTRAK
Portable Particle Counter
04/01/2024
14:42:17
Automatico
phibo sala iso8
Σ m³
µm
312862
0,5
117415
1,0
3138
5,0
Ubicación01
Tiempo:
00:01:00
Demora:
00:00:15
Volumen:
32,5 L
Conteo:
1/1
Regs:
20/10000
Principal
Configurar
Datos
Reportes

Categoría 2 CSPs: 4 Aspectos

Shorter

BUD assignment

Longer

Compounding Method	Sterility Testing	Sterility of Starting Components	Storage Conditions
Aseptically prepared	Sterility testing not performed & passed	One or more nonsterile starting component	Controlled Room Temperature (20-25° C)
Terminally sterilized	Sterility testing performed & passed	Only sterile starting components	Refrigerator (2-8° C)
			Freezer (-25 to -10° C)

Compounding Method	Sterility Testing	Sterility of Starting Components	Storage Conditions	BUD Assignment
Aseptically Prepared	Sterility testing not performed & passed	One or more nonsterile starting component	Controlled Room Temperature (20-25 °C)	4 days
			Freezer (-25 to -10 °C)	45 days

Shorter

ment

En aquellos casos en los que un servicio de farmacia realice preparaciones estériles de stock en número superior al establecido o asigne plazos de validez superiores a los establecidos sin disponer de la justificación documental deberá realizar el test de esterilidad del producto terminado por cada lote fabricado.

NIVEL DE RIESGO Y REQUISITOS DE LA PREPARACIÓN / CONSERVACIÓN

Nivel de riesgo	Requisitos de preparación	Requisitos de conservación [1]
Si el conjunto de letras contiene al menos una D, la preparación se considera una **preparación de riesgo alto**	Servicio de farmacia. Preparación bajo cabina de flujo laminar con entorno controlado (sala blanca)	• 24 horas / temperatura ambiente • 3 días / frigorífico (2 °C – 8 °C) • 45 días / congelador (≤ -20 °C) • 90 días / liofilizado
Si el conjunto de letras contiene al menos una C o tres o más B (y no contiene ninguna D), se considera una **preparación de riesgo medio**.	Servicio de farmacia. Preparación bajo cabina de flujo laminar con entorno controlado (sala blanca)	• 30 horas / temperatura ambiente • 9 días / frigorífico (2 °C – 8 °C) • 45 días en congelador (≤ -20 °C) • 90 días liofilizado
Si el conjunto de letras contiene menos de tres B (ninguna C ni D) se considera una **preparación de riesgo bajo**.	Servicio de farmacia. Preparación bajo cabina de flujo laminar con entorno controlado (sala blanca)	• 48 horas / temperatura ambiente • 14 días / frigorífico (2 °C – 8 °C) • 45 días / congelador (≤ -20°C) • 90 días liofilizado
	Servicio de farmacia. Preparación bajo cabina de flujo laminar sin ambiente controlado.	• 12 horas / temperatura ambiente • 24 horas / frigorífico (2 °C – 8 °C) • 7 días / congelador (≤ -20°C)
	Unidad de enfermería en planta, sin ambiente controlado.	• 1 hora / temperatura ambiente, • 1 hora / frigorífico (2 °C – 8 °C) • No congelar

Sterility of Starting Components	Storage Conditions	BUD Assignment
One or more nonsterile starting component	Controlled Room Temperature (20-25 °C)	30 days
Only sterile starting components	Refrigerator (2-8 °C)	45 days
	Freezer (-25 to -10 °C)	60 days

¿Tenemos que seguir las GMPs? ¿los laboratorios la USP797?

TABLA DE MEDICIÓN Y EVALUACIÓN SAS PERSONAL ISO 7							
FECHA	20/10/2023		NIVEL EXIGENCIA			SEGÚN CLIENTE	UNE 171340 Riesgo 2
PARÁMETRO	RESULTADOS VALOR PROMEDIO					NIVEL EXIGENCIA	NIVEL EXIGENCIA
CLASIFICAIÓN DE LA SALA Nº partículas/m³	0,5 µm		#1	52.600	Clase alcanzada: ISO 7	ISO 7 ≤ 352.000	
			#2	53.710			
			#3	49.760			
	5 µm		#1	2.380	Clase alcanzada: ISO 7	ISO 7 ≤ 2.930	
			#2	1.125			
			#3	2.420			
Partículas en Impulsión	Filtro		Malla 0,3 µm	Perímetro 0,3 µm	Eficacia combinada	Penetración inferior a 0,01%	
	#1		4	429	99,997 %		
Confort termo higrométrico	Temperatura (ºC)		21,1 ºC	Temperatura media (ºC)	21,1 ºC	Tª 21±2 ºC	20-26 ºC
			21,1 ºC				
			21,2 ºC				
	Humedad relativa %		58,3 %	Humedad relativa media (%)	58,1 %	HR 35-70 %	HR 40-60 %
			58,0 %				
			57,9 %				
P. Diferencial Relativa	Acceso 1: S. Preparación		+13,0 Pa	P.D. Absoluta exterior	+26,5 Pa	P. Absoluta / exterior +25±3 Pa	Presión relativa > 6 Pa
	Acceso 2: N. Parenteral		-10,5 Pa				
	Acceso 3: Citostáticos		+6,0 Pa				
Caudales de impulsión (m^3/h)		Impulsión #1	146 m^3/h	CAUDAL TOTAL	146 m^3/h	---	---
Volumen y Nº de renovaciones/hora		Volumen sala (m^3)	12,3 m^3	Nº de renov/hora	11,9 ren/h	≥ 30 ren/h	≥ 10 ren/h
Medición de ruido ambiental		#1	61,3 dBA	Medición media	61,4 dBA	Media ≤85 dBA	---
		#2	60,9 dBA				
		#3	62,0 dBA				
Iluminación		#1	846 lux	Medición media	946 lux	≥500 lux.	---
		#2	888 lux				
		#3	1.104 lux				

¿Category 2 CSPs?

Su farmacia realiza CSPs 2 en una sala limpia. El sistema de ventilación (HVAC) falló durante el fin de semana y ha estado completamente apagado durante 2 días, sin embargo, las campanas todavía están funcionando correctamente. ¿Cuáles son los BUD máximos que puede asignar a los CSP elaborados en la sala limpia hasta que se repare el HVAC?

a. Disminuir BUD a 4 horas a temperatura ambiente, 4 horas refrigerado

b. Disminuir BUD a < 12 horas a temperatura ambiente, < 24 horas refrigerado

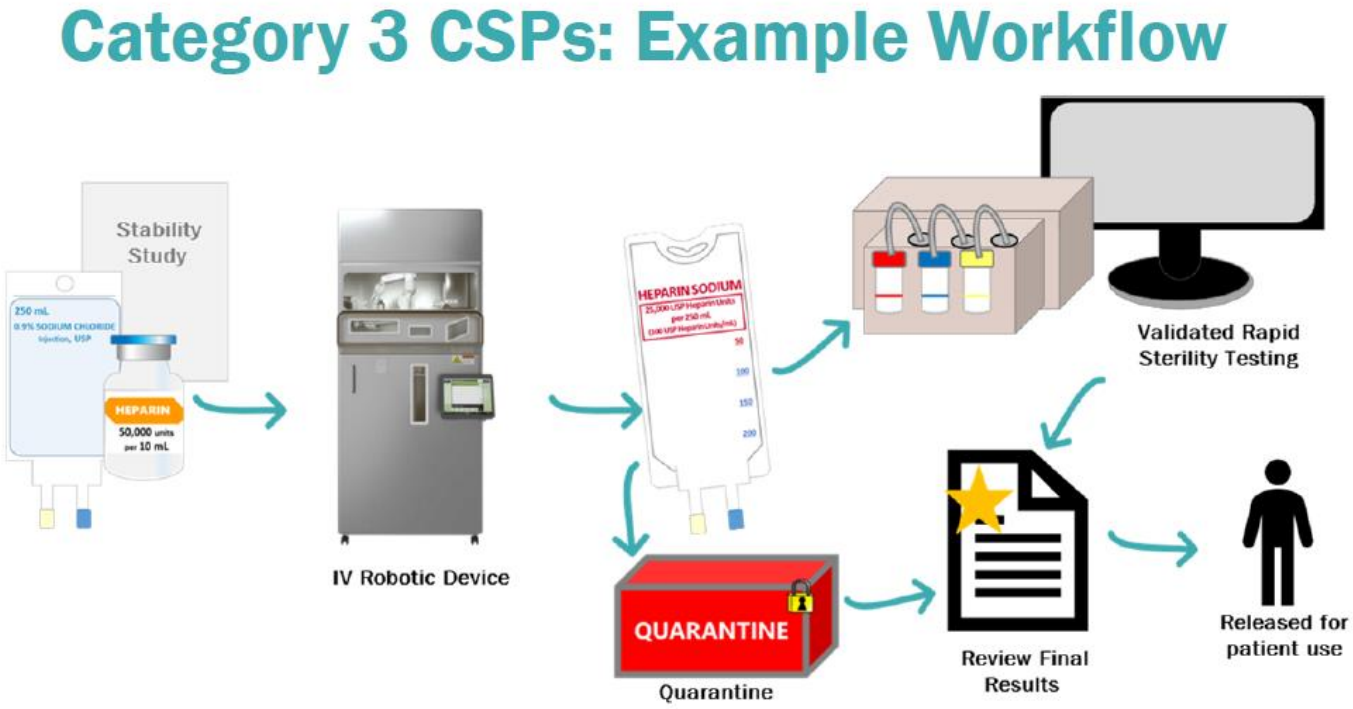
C. Mantener la BUD actual (4 días a temperatura ambiente, 10 días refrigerada, 45 días congelado)

d. Debe dejar de elaborar hasta que se repare el sistema HVAC.

Categoría 3

Quimera…

- Certificaciones de personal cada 3 meses,registro de todos, requisitos de indumentaria muy altos
- (No exposición de piel)
- Robots automáticos básicamente más….



ISMP Y NIOHS: Seguridad

- ¿Sirven las recomendaciones de la ISMP?
- ¿Vale la pena esa cultura de seguridad?
- ¿Pequeños pasos son suficientes?

Para más escépticos

My biggest strategy pet peeves

- Be more careful next time
- Remember

Do you believe that doing *something* is better than doing nothing?

YES

NO

- ¿ Evidencia del tallman lettering ?
  - DOBUtaminna – DOPamina
  - vinBLAStina-vinCRIStina

Clinical evidence of Tall Man's effectiveness ought to have been required prior to widespread implementation."

Tallman studies

- Darker, et al (2011) found that the accuracy in drug name perception was no higher with TALLman lettering when compared to names listed in all uppercase format.
- Zhong, et al (2015) found no measurable effect on drug name confusions in 9 years of data from 42 children's hospitals.
- Larmené-Beld, et al (2018) found in a systematic review that medication error rates ranged from 3 to 22% for Tall Man lettering and from 3 to 24% for non-Tall Man lettering.

¿Colores?

Are you color blind?

- FREE test: https://enchroma.com/pages/test
- 1/12 men; 1/200 women
- Types of color blindness:
  - red - green
  - blue - yellow
    - blue - green AND ye
    - blue - green AN
  - complete

- Sesgo de confirmación:
  - VEMOS LO QUE ESPERAMOS VER
- O sea ,tendemos a buscar información que respalda los puntos de vista que tienes o lo que ya crees en este caso

The truth about independent double checks

1. not supported by evidence
2. rarely properly conducted / rarely defined
3. have costs that may not be appreciated

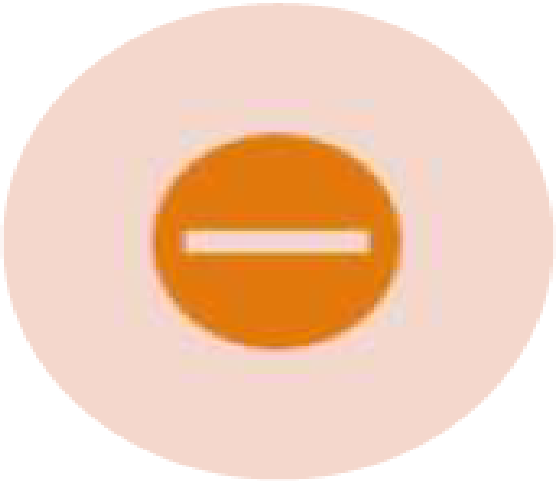
No te conformes

- Y RARAMENTE SE HACEN BIEN

Inducen fallos de procedimiento
Bien hechos son caros en tiempo, esfuerzo y dinero
Mal hechos promueven la “normalización de la desviación”: genera indiferencia a las normas

Do you believe that doing *something* is better than doing nothing?

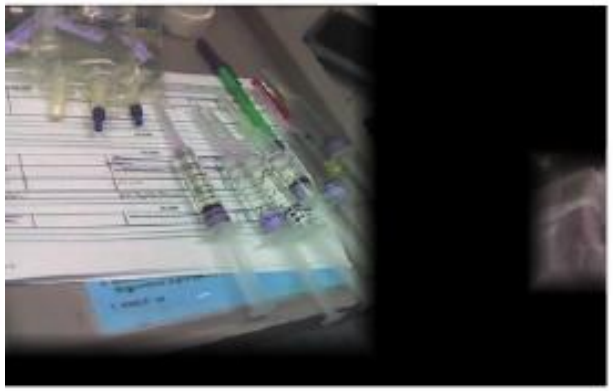
YES



(PLEASE SAY) NO!

Mira fuera de tu servicio

What's Behind the Double Doors?



Look where you really don't want to look

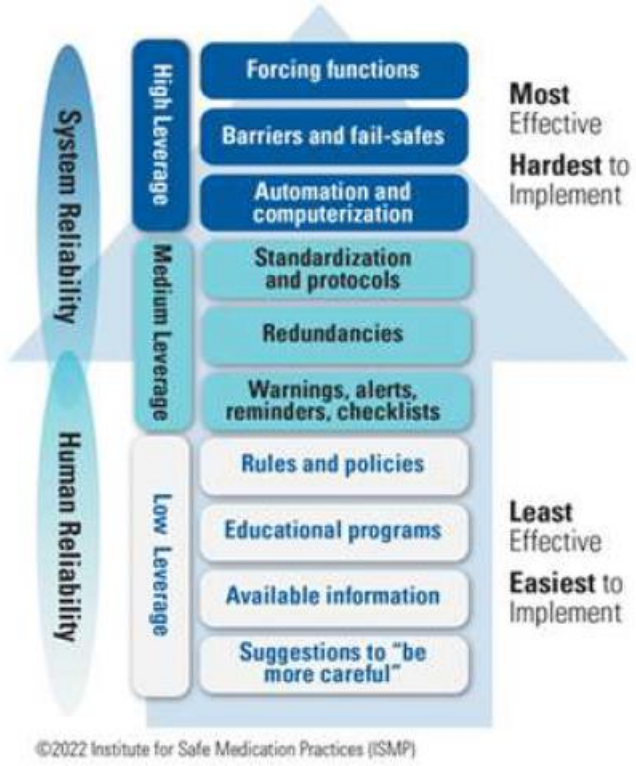
Guaranteed there's stuff out there you don't know about

- Look for:
  - Kits
  - Boxes
  - Trays
  - Bags
  - Drugs attached to walls, carts, etc.

Mensajes clave

- Mira todos los lugares, no solo tu farmacia, Conoce los riesgos que existen fuera
- Se busca la fiabilidad del sistema
- Implementa medidas de alta eficacia: NO TE CONFORMES con “hacer algo”

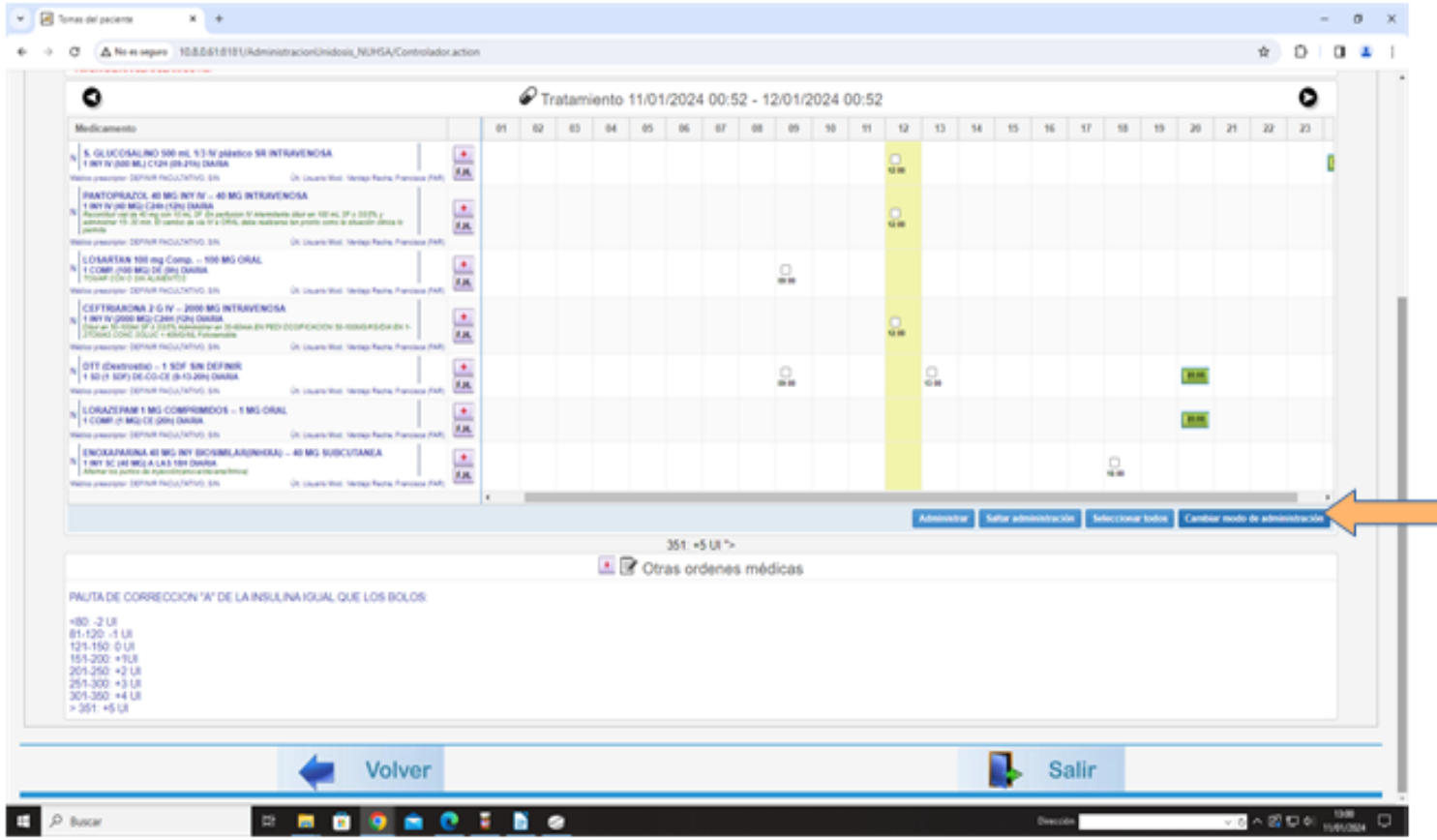
Make it easy to do the right thing and nearly impossible to do the wrong thing.



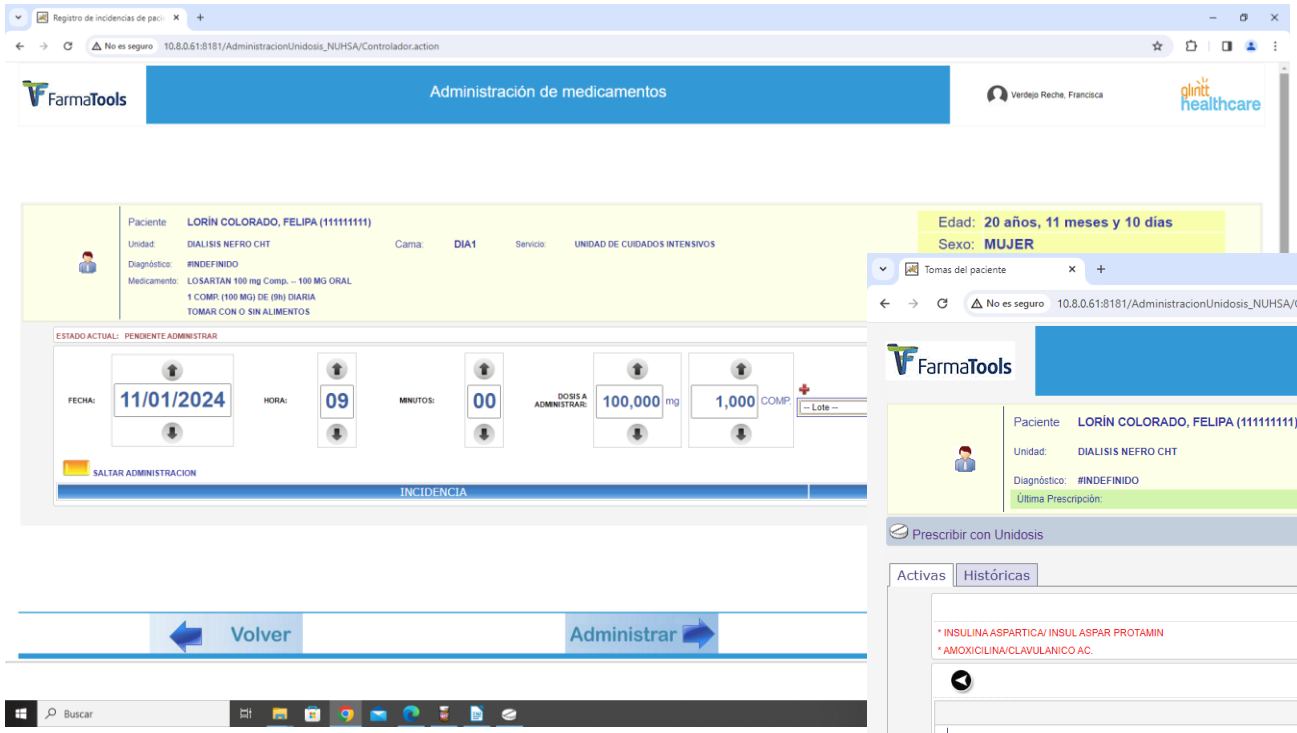
High-level strategies

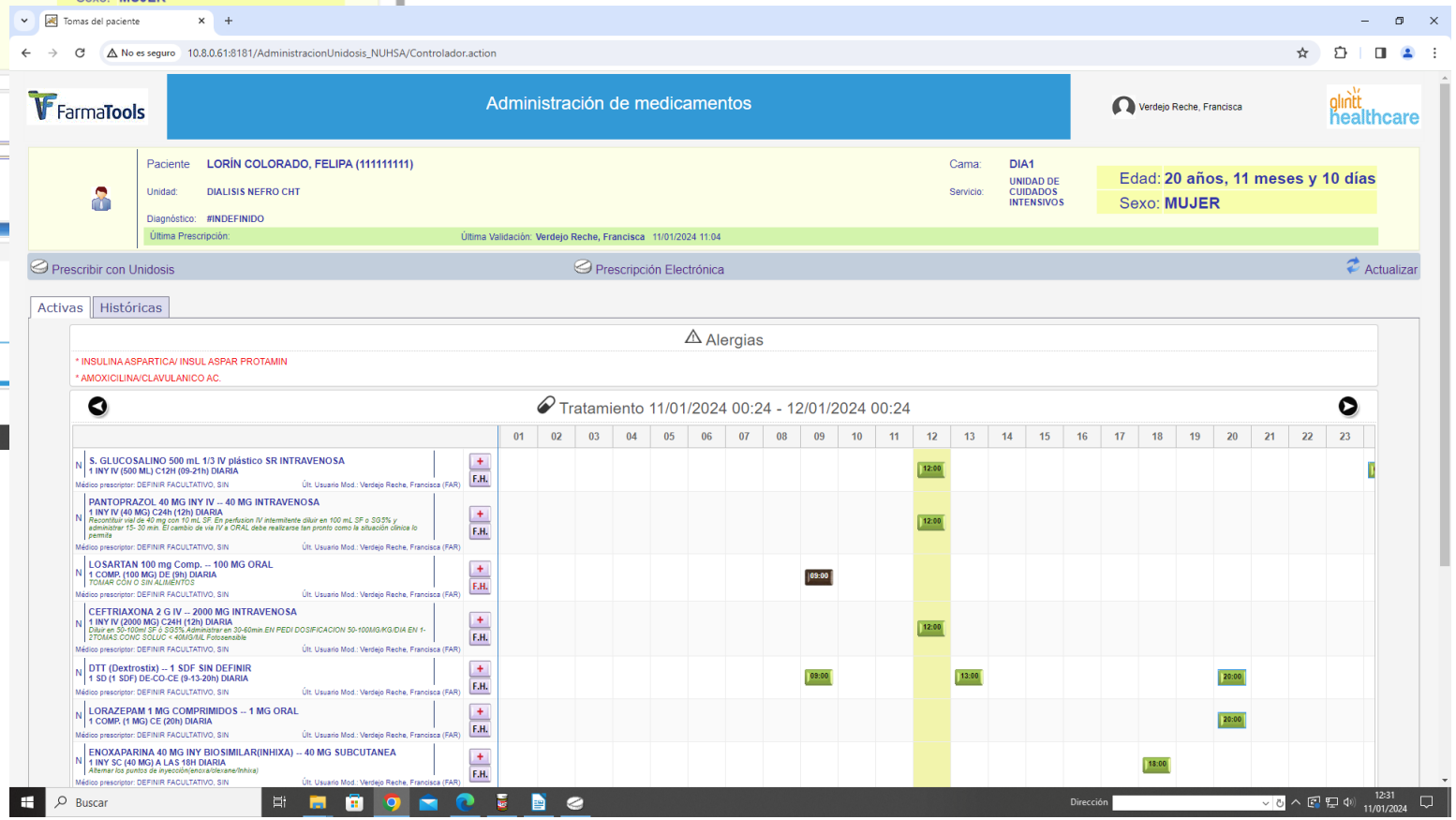
- Automation
- Standardization
- Bar coding
- Prescriber order entry settings
- Smart pumps
- DERS (dose error reduction software)

Me ha motivado



Se seleccionan los medicamentos y se administran a la vez.


Registro de incidencias de paci
No es seguro
10.8.0.61:8181/AdministracionUnidosis_NUHSA/Controlador.action
FarmaTools
Administración de medicamentos
Verdejo Reche, Francisca
glintt healthcare
Paciente LORÍN COLORADO, FELIPA (111111111)
Unidad: DIALISIS NEFRO CHT
Cama: DIA1
Servicio: UNIDAD DE CUIDADOS INTENSIVOS
Diagnóstico: #INDEFINIDO
Medicamento: LOSARTAN 100 mg Comp. -- 100 MG ORAL
1 COMP. (100 MG) DE (9h) DIARIA
TOMAR CON O SIN ALIMENTOS
Edad: 20 años, 11 meses y 10 días
Sexo: MUJER
ESTADO ACTUAL: PENDIENTE ADMINISTRAR
FECHA: 11/01/2024
HORA: 09
MINUTOS: 00
DOSIS A ADMINISTRAR: 100,000 mg
1,000 COMP.
-- Lote --
SALTAR ADMINISTRACION
INCIDENCIA
Volver
Administrar
Buscar


Tomas del paciente
No es seguro
10.8.0.61:8181/AdministracionUnidosis_NUHSA/Controlador.action
FarmaTools
Administración de medicamentos
Verdejo Reche, Francisca
glintt healthcare
Paciente LORÍN COLORADO, FELIPA (111111111)
Unidad: DIALISIS NEFRO CHT
Diagnóstico: #INDEFINIDO
Cama: DIA1
Servicio: UNIDAD DE CUIDADOS INTENSIVOS
Edad: 20 años, 11 meses y 10 días
Sexo: MUJER
Última Prescripción:
Última Validación: Verdejo Reche, Francisca 11/01/2024 11:04
Prescribir con Unidosis
Prescripción Electrónica
Actualizar
Activas
Históricas
Alergias
* INSULINA ASPARTICA/ INSUL ASPAR PROTAMIN
* AMOXICILINA/CLAVULANICO AC.
Tratamiento 11/01/2024 00:24 - 12/01/2024 00:24
01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23
S. GLUCOSALINO 500 mL 1/3 IV plástico SR INTRAVENOSA
1 INY IV (500 ML) C12H (09-21h) DIARIA
PANTOPRAZOL 40 MG INY IV -- 40 MG INTRAVENOSA
1 INY IV (40 MG) C24h (12h) DIARIA
LOSARTAN 100 mg Comp. -- 100 MG ORAL
1 COMP. (100 MG) DE (9h) DIARIA
TOMAR CON O SIN ALIMENTOS
CEFTRIAXONA 2 G IV -- 2000 MG INTRAVENOSA
1 INY IV (2000 MG) C24H (12h) DIARIA
DTT (Dextrostix) -- 1 SDF SIN DEFINIR
1 SD (1 SDF) DE-CO-CE (9-13-20h) DIARIA
LORAZEPAM 1 MG COMPRIMIDOS -- 1 MG ORAL
1 COMP. (1 MG) CE (20h) DIARIA
ENOXAPARINA 40 MG INY BIOSIMILAR(INHIXA) -- 40 MG SUBCUTANEA
1 INY SC (40 MG) A LAS 18H DIARIA
Médico prescriptor: DEFINIR FACULTATIVO, SIN
Últ. Usuario Mod.: Verdejo Reche, Francisca (FAR)
F.H.
Buscar
Dirección
12:31
11/01/2024

Strategies for Risk Mitigation

In the literature:
Pharmacy prepared pre-filled syringes and pre-mixed infusions of frequently used high alert medications reduced Medication Errors 17-fold.

- Prefilled Syringes/Premixed Infusions
- Pharmacy compounding/dilution
- Consolidate formulary and preference lists
- Barcode assisted syringe label printers
- Multidisciplinary sterile compounding education and training

2022: 3 prácticas nuevas

a) “Salir de la hospitalización “ para implanter código de barras

b) Medicamentos de alto riesgo: procesos

2022 New Best Practices *Baseline* Survey

Expand use of barcode scanning technology

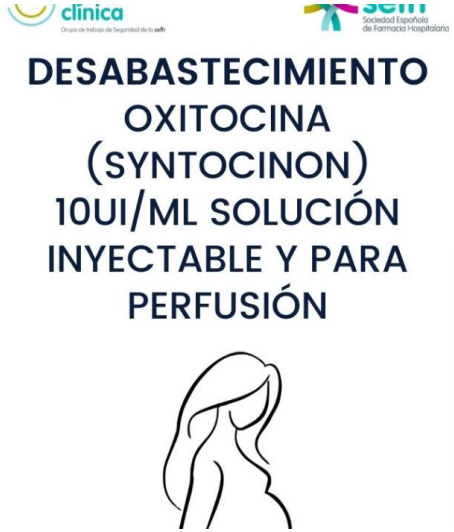
- 76% infusion clinics
- 73% post anesthesia care
- 72% labor and delivery
- 67% dialysis
- 65% emergency department

Target clinical areas with a short or limited patient stay

2022 New Best Practices *Baseline* Survey

Safe use of high-alert medications

- 64% • Create a robust set of processes for managing risk
- 63% • Addressing vulnerabilities at each stage of the process
- 51% • Avoid relying only on low-leverage risk-reduction strategies
- 66% • Limit the use of independent double checks
- 69% • Regularly assess for risk from internal and external sources
- 41% • Establish outcome and process measures



Nuevas Mejores Prácticas :

ISMP 2024-2025 *Targeted Medication Safety Best Practices for Hospitals*

1, Safeguard against wrong-route errors with tranexamic acid

¿Cuál o cuales de estas afirmaciones son verdaderas respecto al uso erróneo de la vía de administración del ácido tranexámico?
a. Son frecuentes y producen un daño moderado
b. Está disminuyendo su incidencia
c. La mayoría de los casos se debe a su similitud con otros medicamentos

2, Implement strategies to prevent medication errors at transitions in the continuum of care.

3, Safeguard against errors with vaccines administered in the inpatient and associated outpatient settings

- El ácido tranexámico es un antifibrinolítico utilizado para controlar el sangrado.
- Cuando se administra accidentalmente por vía neuroaxial, es una potente neurotoxina.
- La tasa de mortalidad con tales errores es de alrededor del 50%.
- Casi siempre deja secuelas. Los supervivientes a menudo experimenta convulsiones, daño neurológico permanente y paraplejía.

¿Qué es verdad respecto al uso erróneo de la vía de administración del ácido tranexámico?

a. Son muy frecuentes y producen un daño moderado

b. Está disminuyendo su incidencia

c. La mayoría de los casos se debe a su similitud con otros medicamentos

- Si es posible NO almacenar tranexámico en la bandeja de anestesia
- Separa o secuestra el almacenaje del mismo: Asegúrate que tiene pocas localizaciones y que no está cerca de anastésicos locales
- Evita almacenar viales de pie, para evitar la confusión viendo sólo la tapa del vial, sobretodo si se guardan en cajón o bandeja debajo de la línea de visión . ETIQUETAS VISIBLES
- Considera etiquetar las tapas con etiqueta: CONTIENE TRANEXÁMICO

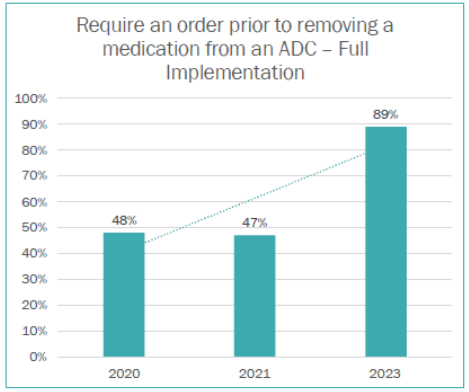
- Haz una revisión para identificar ampollas y viales look-alike por el riesgo de confundirlos al mezclarlos ; REVÍSALO AL CAMIBAR DE MARCAS (si es que se puede elegir) : DESABASTECIMIENTOS.
- Usa códigos de barra previos a la administración del medicamento en áreas quirúrgicas y obstétricas .
- Cuando sea apropiado, usar mezclas preparadas de tranexámico con cloruro sódico (estilo vincristina)

¿Sirven las recomendaciones de la ISMP?

Para escépticos

Measuring Progress – Most Implemented

- Require a medication order prior to removing any medication from an ADC, including those removed via override.



ADC: automated dispensing cabinet

ashp MIDYEAR 2023

"Lo Positivo"

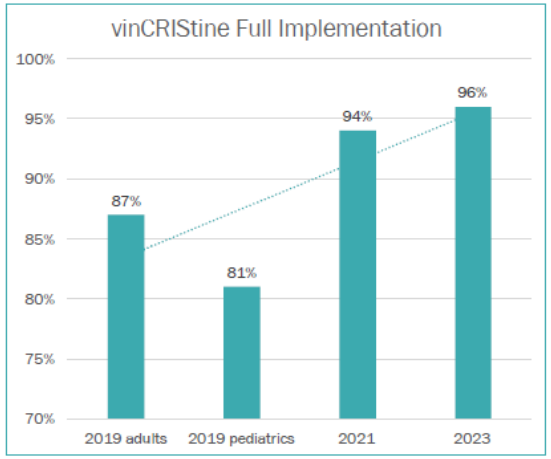
- Sino se mide, no sabe si se mejora
- En mayor o menor medida se mejora

¿Sirven las recomendaciones de la ISMP?

Para escépticos

Measuring Progress – Most Implemented

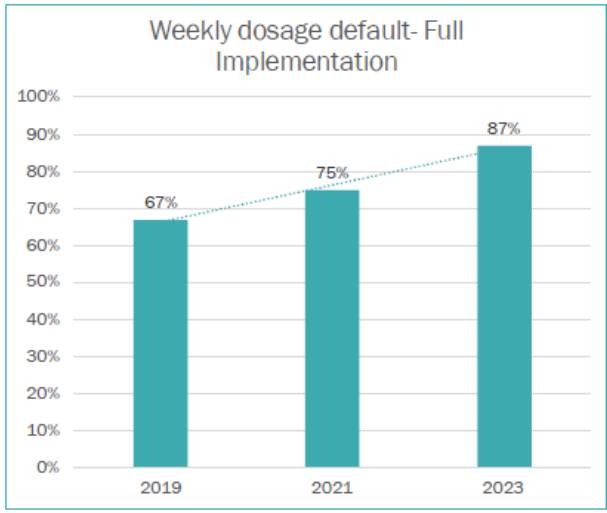
- Dispense vinCRIStine and other vinca alkaloids in a minibag of a compatible solution and not in a syringe.



"Lo Positivo"

Measuring Progress – Most Implemented

- Use a weekly dosage regimen default for oral methotrexate orders.

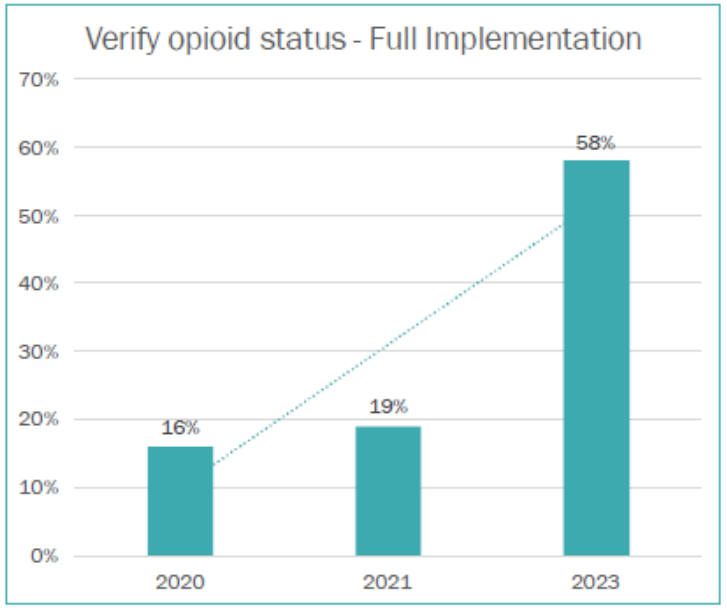


Recomendaciones ISMP: aún queda por hacer

“Lo negativo/mejorable”

Opportunities – Least Implemented

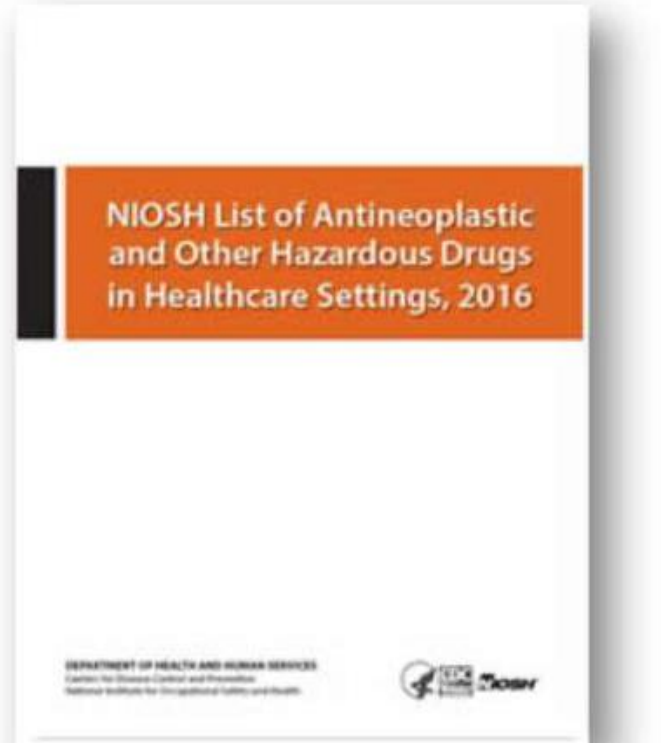
- Verify/document a patient’s opioid status and pain type before prescribing/dispensing extended-release or long-acting opioids
- *Keys:* adding a hard stop for providers; adding assessment questions on order entry; defining tolerance for pediatric population



Polling Question

Which of the following is the most current "final" NIOSH list?

1. NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016
2. NIOSH List of Hazardous Drugs in Healthcare Settings, 2020
3. NIOSH Alert! Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings, 2004
4. NIOSH List of Hazardous Drugs in Healthcare Settings, 2023
5. NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2018



HAZARDOUS DRUG EXPOSURES IN HEALTHCARE

Print

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016
DHHS (NIOSH) Publication Number 2016-161

Managing Hazardous Drug Exposures: Information for Healthcare Settings
DHHS (NIOSH) Publication Number 2023-130 (April 2023)

NIOSH list

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016

https://www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf?id=10.26616/NIOSHPUB2016161

Managing Hazardous Drug Exposures: Information for Healthcare Settings

https://www.cdc.gov/niosh/docs/2023-130/2023-130.pdf?id=10.26616/NIOSHPUB2023130

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

		Control Approaches						
		Engineering Controls			Personal Protective Equipment			
Activity	Formulation	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemo-therapy gloves (ASTM rated)	Pro-tective gown (imper-vious, single use)	Eye, face, hair, sleeve, and shoe protection	Respiratory protection†
Compounding‡	Oral liquid drug	Yes§	NA*	NA*	Yes¶	Yes	Hair and shoe covers; Add eye and face pro-tection, if not done in a ventilated engineer-ing control	Yes, if not using a ventilated engineering control
	Topical drug	Yes§ (Note: some drugs such as carmustine, thiotepa, and mechlore-thamine are volatile)	NA*	NA*	Yes¶	Yes	Hair and shoe covers. Add eye and face pro-tection, if not done in a ventilated engineer-ing control	Yes, if not done using a ventilated engineering control
	Injections withdrawn from a vial	Yes§	Yes, when dosage form allows	NA*	Yes¶	Yes	Hair and shoe covers; Add eye and face pro-tection, if not done in a ventilated engineer-	Yes, if not using a ventilated engineering

Compounding

Oral liquid drugs

Controls: Ventilated engineering control (fume hood or Class 1 BSC, CVE, or CACI).

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and respiratory protection (N95) if compounding is done outside of the ventilated engineering control. Hair and shoe covers should be worn.

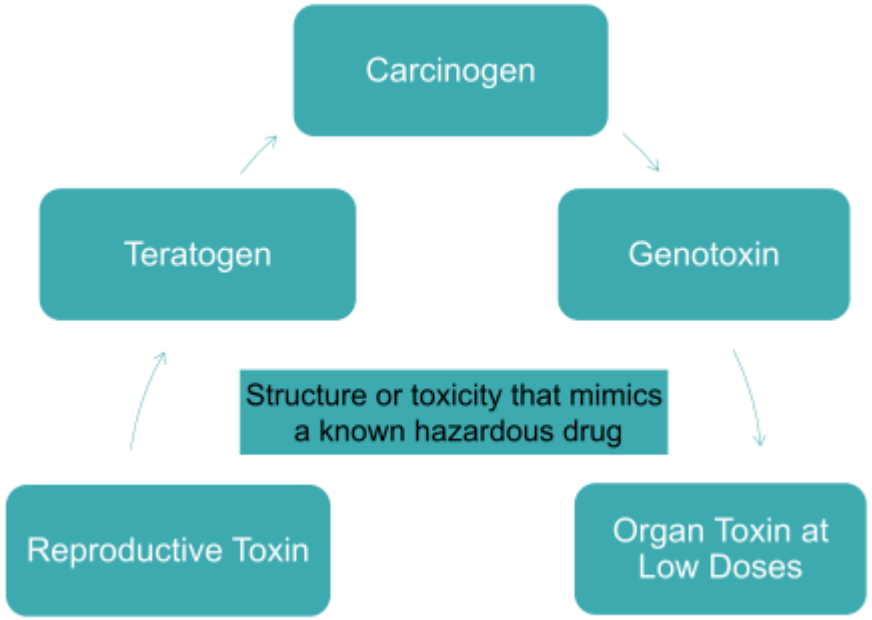
Definición HD

2023 NIOSH Changes — Criteria

- 1: Aprobado en humanos (CDER) y no regulado de otra forma Y
- 2a : lo indica el fabricante: MSHI: Manufacturer Special Handling Information O
- 2b : Cumple previos criterios NIOSH

NIOSH additional criteria:

- "Structure/toxicity profile of new drugs that mimic existing hazardous drugs"



Porque no es lo mismo daño que el riesgo

- Group 1: Antineoplastic drugs, defined as AHFS classification 10:00
- Group 2: Non-antineoplastic drugs that meet other NIOSH criteria as hazardous
- Group 3: Drugs with reproductive risk or may be present in breast milk

Pasará de 3 grupos (o tablas) a 2 más observaciones

- Tabla 1: MSHI o cumple criterios NIOSH Y
  - NTP carcino o ”razonablemente carcinogénico en humanos”
  - IARC grupo 1 (carcinogénico) o 2a (probablemente carcinogénico)
- Tabla 2: cumple criterios NIOSH y
  - No MSHI
  - No en los grupos IARC o NTP anteriores

NIOSH 2020-¿24?

CAMBIOS

Grupo 1

- Medicamentos carcinógenos
- Medicamentos MSHI

No todos los medicamentos incluidos son antineoplásicos

Grupo 2

- Medicamentos cumplen criterio NIOSH/No carcinógenos
- Medicamentos riesgo desarrollo/reproducción

No incluye medicamentos MSHI
Se incluyen medicamentos que solo suponen riesgo en la reproducción o desarrollo

Grupo 3

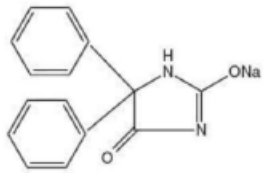
Los medicamentos de la grupo 3 pasan a considerarse del grupo 2

- USP 800: Solo los antineoplásicos fármacos en la tabla 1 requerirán cumplirlo COMPLETAMENTE
  - Se establecerá el riesgo de forma individual si
    - Manipulas fármacos no antineoplásicos de la tabla 1
    - Manipulas fármacos antineoplásicos de la tabla 2
    - Fármacos comercializadas tras la publicación de la última NIOSH (tu organización debe aplicar los criterios NIOSH y decidir si tratarlos como HD)

¿Cómo manejáis esta medicación?

Applying USP <800> and the NIOSH List

Example 1: Small-molecule drug



- Table 2 on current NIOSH list
- Not AHFS 10:00
- IARC Group 2B
- NTP “reasonably anticipated to be carcinogen”
- Evaluating commercially available sterile injection and also solid and oral liquid dosage forms

-
- Se debe establecer el riesgo porque está en la tabla 2 de la lista NIOSH
- Estableces el riesgo porque no es una droga antineoplásica
- FENITOÍNA

NIOSH List of Hazardous Drugs in Healthcare Settings, 2020

NIOSH 2016

GRUPO 1	GRUPO 2
Altretamina, amsacrina, azacitidina, Azatioprina, belinostat, bendamustina,	Abacavir, abiraterona, acitretina, afatinib, aflibercept, alefacept,

Table 2 (Continued). Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug, including those with the manufacturer's safe-handling guidance (MSHG)

Drug	AHFS classification	MSHG	Supplemental information	Links
palifermin	84:16 cell stimulants and proliferants		FDA Pregnancy Category C; potential for stimulation of tumor growth	DailyMed; DrugBank
paliperidone	28:16:08:04 atypical antipsychotics		Metabolite of risperidone; excreted in human breast milk; FDA Pregnancy Category C	DailyMed; DrugBank
phenoxybenzamine	12:16:04:04 non-selective alpha-andrenergic blocking agents		IARC Group 2B; FDA Pregnancy Category C	DailyMed; DrugBank
phenytoin	28:12.12 hydantoins		IARC Group 2B; NTP***; FDA Pregnancy Category D	DailyMed; DrugBank

Estabilidad físico química Fenitoína diluida

JOURNAL ARTICLE

Compatibility and pH variability of four injectable phenytoin sodium products

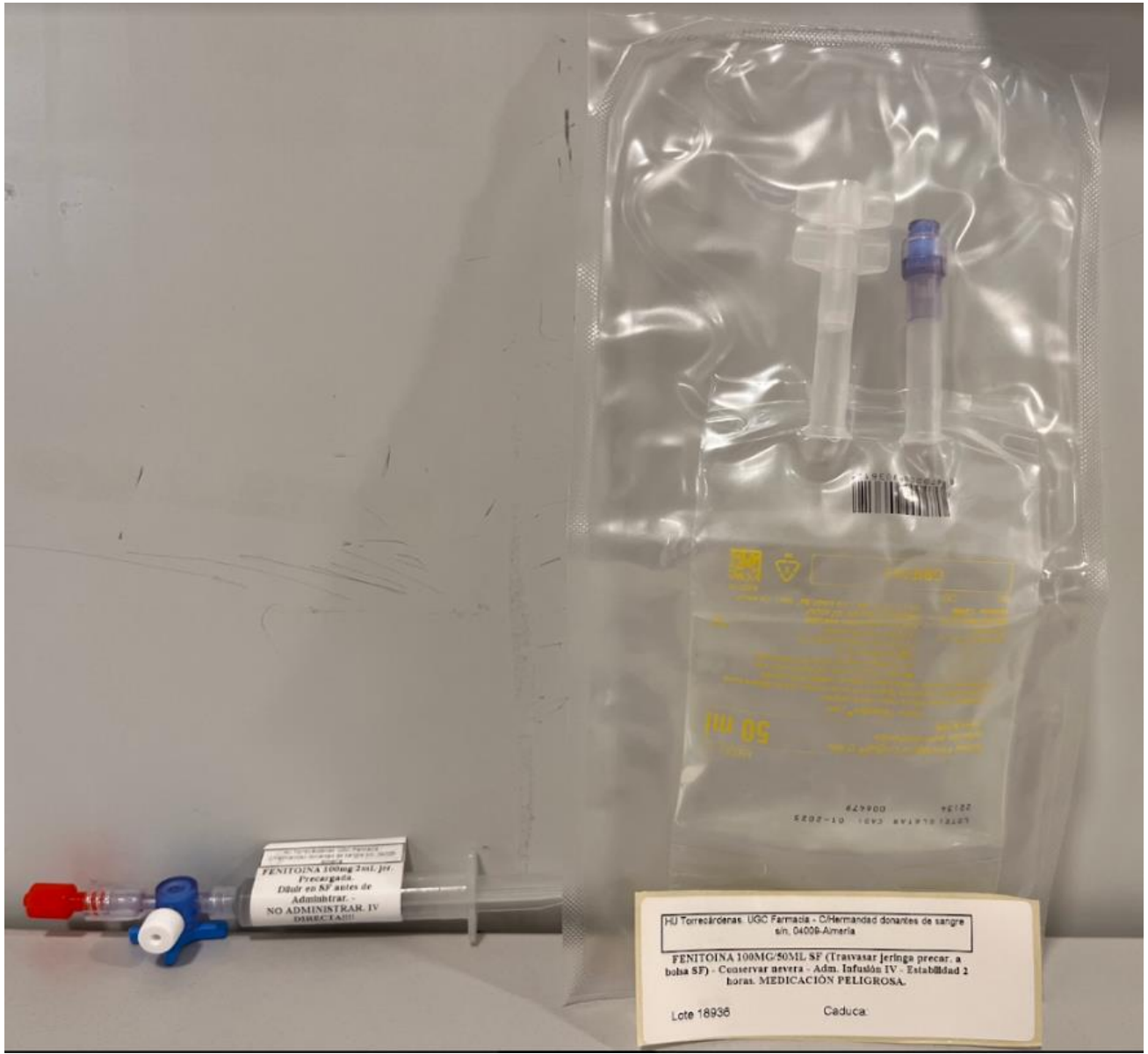
Get access >

Susan J. Markowsky, PHARM.D. ✉, Philip R. Kohls, PHARM.D., David Ehresman, M.T., Ilo Leppik, M.D., MINCEP Epilepsy Care PA

American Journal of Hospital Pharmacy, Volume 48, Issue 3, 1 March 1991, Pages 510–514,
https://doi.org/10.1093/ajhp/48.3.510
Published: 01 March 1991

Interlot variability in pH was lowest for Dilantin, and apparent pH values of the undiluted products and in the admixtures at both drug concentrations were significantly higher for Dilantin than for the other products. Microscopic evidence of physical incompatibility was noted in some generic product lots with lower apparent pH values. Stability of phenytoin in the admixtures over two hours was demonstrated for all four phenytoin sodium injectable products studied.

Qué hacemos



LABORATORIO MICROBIOLOGÍA

MICROBIOLOGÍA (Cultivo y microscopía)

Control de esterilidad (farmacia)

Cultivo general (control de esterilidad) **Informe Final**	**No desarrollo bacteriano en 5 días**	WSR

HU Torrecárdenas. UGC Farmacia - C/Hermandad donantes de sangre s/n, 04009-Almería

FENITOINA 100MG/50ML SF (Trasvasar jeringa precar. a bolsa SF) - Conservar nevera - Adm. Infusión IV - Estabilidad 2 horas. MEDICACIÓN PELIGROSA.

Lote Caduca:

HU Torrecárdenas. UGC Farmacia - C/Hermandad donantes de sangre s/n, 04009-Almería

FENITOINA 100mg/2mL jer. Precargada.
Diluir en SF antes de Administrar. -
NO ADMINISTRAR. IV DIRECTA!!!!

Q18/18936 Cad: 31/03/24(2-8ºC)

Mensajes Finales

- Seguridad CV : FOMENTAR ADHERENCIA enseñando el riesgo
- Nueva USP 797 :
  - Somos hospitales, no fabricantes
  - Centralizar Y HOMOGENEIZAR mezclas
- ¿Nuevas? Recomendaciones ISMP: No te conformes
- Nueva ¿NIOSH?/USP 800: Sírverte de ello para centralizar

My 2024 Work Goal