



London Health Sciences Centre



The BD Issue What? So What? Now What?

CSHP PPC
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Presenter Disclosure

I have no current or past relationships with commercial entities

Commercial Support Disclosure

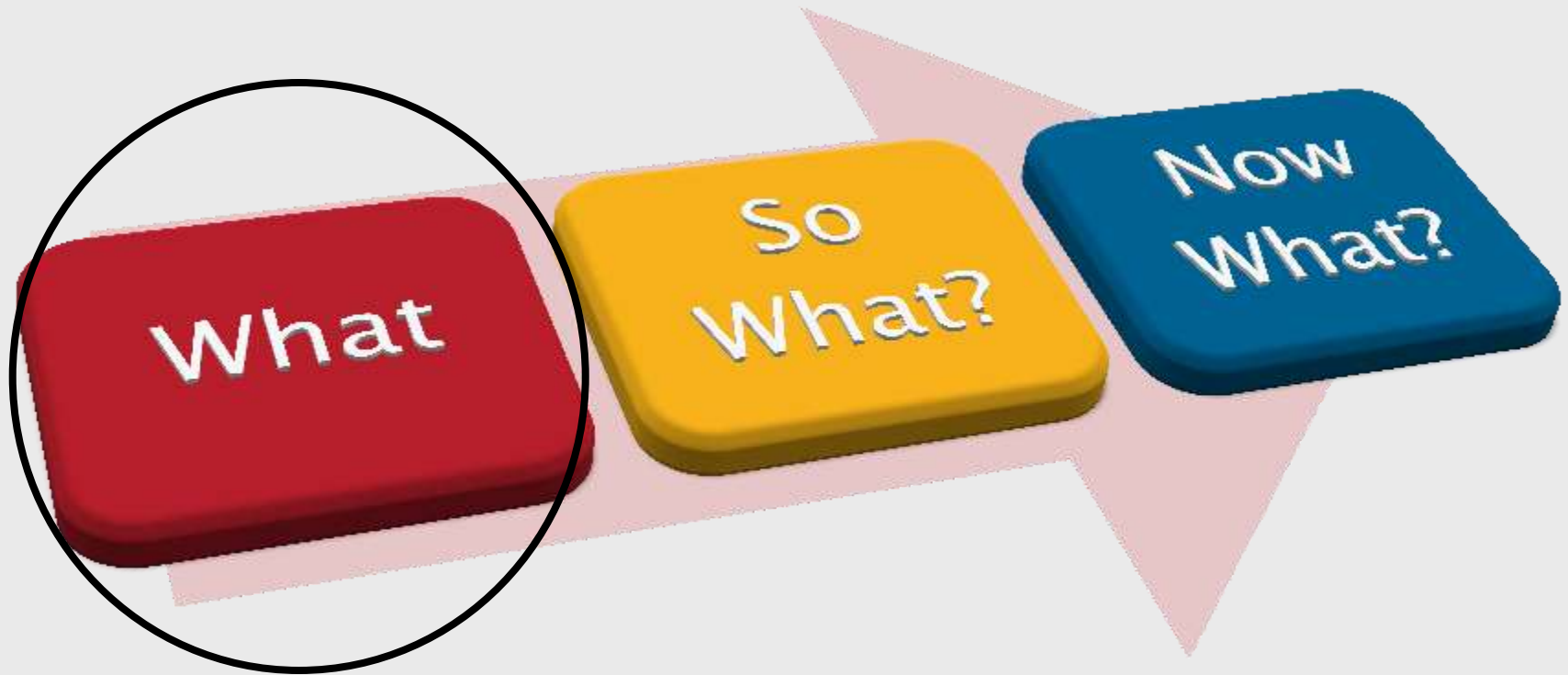
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Objective

- 1. What do we know?*
- 2. What don't we know?*
- 3. What do we wish we knew?*
- 4. Now what?*





Timeline – US

July 30 – ISMP US Special Alert

- *Loss of drug potency reported in 3 and 5mL BD syringes when prepared in advance of administration*

July 31 – BD Letter to Customers

- *Reports of reduced potency with ‘certain’ medications*

August 18 – FDA Alert

- *10, 20 and 30ml also contain same rubber – Evaluate Use*

August 27 – ISMP US Follow Up

- *May be related to secondary rubber*
- *BD Syringes not approved for drug storage (FDA)*
- *Need to administer drugs promptly*

Timeline – US

Sept 1 – BD Letter to US Customers

- Aware syringes are being used ‘Off Label’
- Drug list provided

Sept 8 – FDA Expands Alert to 10, 20 and 30ml BD syringes

Timeline – Canada

August 31 – BD notifies Canadian customers !!

- fentanyl, rocuronium, neostigmine, morphine, midazolam, methadone, atropine, hydromorphone, cisatracurium, and remifentanyl.
- Decreased drug potency has only been reported when drugs are stored in these syringes.
- BD general purpose syringes have been Health Canada cleared for fluid aspiration and administration only, and not for drug storage.

Sept 18 – OCP

- A review of current practices in this area must be undertaken, and any necessary adjustments to policies and procedures should be made to minimize ongoing risk to patients and enhance the safe and effective delivery of pharmacy services.
- Working Group established

Timeline – Canada

Sept 23 – Health Canada Issues Alert

- Affected lots include: 3 mL, 5 mL, 10 mL and 30 mL BD syringes, and BD oral/enteral syringes
- Healthcare professionals should confirm that BD syringes used for compounding or repackaging drugs do not contain the alternate stopper associated with this issue
- Compounded or repackaged drugs that have been stored in the affected lots of syringes should not be administered unless there is no suitable alternative available.



WHAT do we REALLY know??

Case Reports:

- Syringes filled with fentanyl citrate 10 mcg/mL by a hospital pharmacy retained only 67% potency after 48 hours of storage and 55% potency after 6 days of storage according to laboratory analysis.
- In a separate analysis, 3mL syringes filled with fentanyl citrate 5 mcg/mL from a different hospital pharmacy retained 10% to 70% potency. Confirmed by two other labs.

WHAT do we REALLY know??

Case Reports cont'd:

- Inadequate analgesia from fentanyl was reported by a third hospital pharmacy using these syringes for prolonged storage (> 24 hours).
- Inadequate neuromuscular blockage with rocuronium stored in 5mL BD syringes was reported from another hospital.

WHAT do we REALLY know???

- To date, decreased potency has been reported for the following drugs: fentanyl, rocuronium, neostigmine, morphine, midazolam, methadone, atropine, hydromorphone, cisatracurium, and remifentanyl.
- Syringes are classified by Health Canada as Medical Devices. BD general purpose syringes have been approved by Health Canada for fluid aspiration and administration only, and not for drug storage.

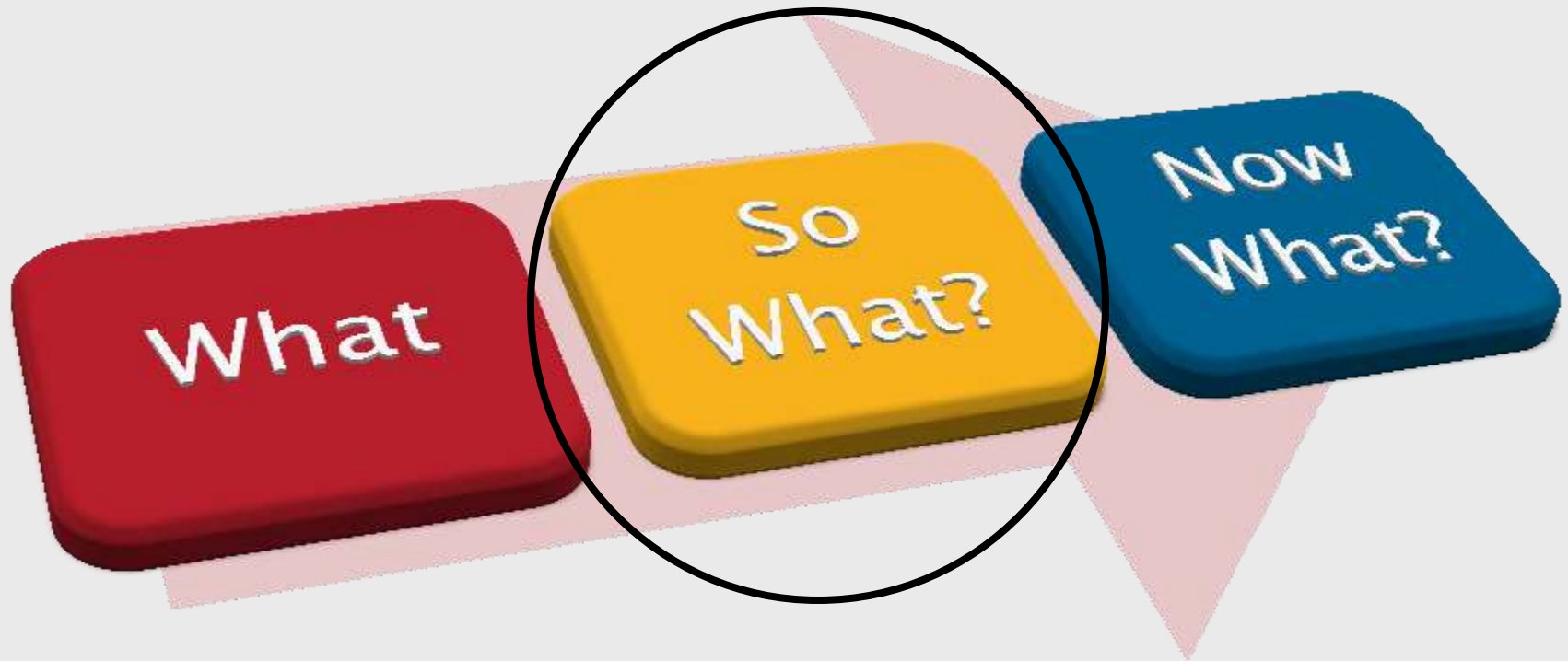
WHAT do we REALLY know??

- The components and processes used to manufacture a syringe are subject to change. Provided the syringe remains fit for its purpose (as per its market authorization), syringe manufacturers are not required to notify customers of changes in their product specifications.
- The secondary or affected rubber has been distributed to the Canadian market since 2013.
- The USP has established that the acceptable range of potency for an active pharmaceutical ingredient preparation is typically $\pm 10\%$,

What we DON'T know

- What exactly is the potency loss and how quickly does it happen for the reported drugs?
- What was the concentration of the product and diluent used in products where there was a problem?
- What other drugs may be affected if packaged in a syringe containing the secondary/affected rubber?
- What is the mechanism for the concentration loss?
- What type of rubber was used in published studies testing the stability of drugs? Is this data valid still given the new information regarding syringe composition changes?
- What does “PROMPT administration” mean?
- Is this issue limited to syringes manufactured by BD or does it extend to other manufacturers?





So What???

No Syringe Is Approved as a Standalone Storage Container!

The seemingly common practice at pharmacies and outsourcing facilities of storing sterile compounded preparations or repackaging sterile pharmaceuticals in drug-administration syringes is actually an unapproved use of these medical devices.



We have two choices?

- 1) Test every drug at every concentration that you use and in every size syringe that you use OR
- 2) Rely on the results of published stability studies “if you have the exact same syringe, the exact same concentration, the exact same manufacturing environment and the exact same drug and you . . . handle it and store it just like the drug in the study was stored.”

BUT...



Fun Fact...

Specific to these products, manufacturing changes that do not result in either a change to intended use or classification of a product, do not require notification or approval by Health Canada.



now
what?

OCP Working Group

Membership:

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“Quality is never an accident; it is always the result of high intention, sincere effort, intelligent direction and skillful execution; it represents the wise choice of many alternatives.”

William A. Foster

Goals

The Syringes as Medications Storage (SaMS) Device Working Group will evaluate the current situation and make recommendations regarding the appropriate management of this situation given the new information provided by the syringe manufacturer.

Deliverables

Short Term (within 1 month)

- Complete an environmental scan to assess current practice relating to medication storage in hospitals across Ontario.
- Utilizing the Ethical Framework and the principles of risk/benefit analysis, conduct a risk assessment of current practice of medication storage based on information currently available,
- Provide recommendation/guidance to hospital pharmacies relating to management of risk in the short term.
- Continue to work the Health Canada, FDA, BD and others to obtain information regarding the drug concentration changes that have been reported and the suspected mechanism for the change.

Deliverables

Mid– Term (within 3 months)

- Develop a plan to obtain the required data to complete a thorough risk assessment
- Working with CSHP and ISMP Canada, develop guidelines for drug packaging and storage that take into consideration the evolving nature of this situation and an assessment of the validity of currently published information.

Long Term (one year)

- Work with regulatory bodies (e.g. Health Canada) to develop required changes in legislation (e.g. licensed medical device for drug storage).

Seems Simple...

$$\begin{array}{l} 1 + 1 = 2 \\ 1 + 2 = \\ 2 + 2 = \end{array}$$



**not so
much**

We still don't know...much



So how do you make a recommendation?



- If syringe components change frequently, can we ever rely on stability testing?
- Could we standardize compounding so testing would be feasible?
- Will there be an approved storage device?
- Can hospitals provide “just in time” product efficiently?

Turns out...Trissel was Right!

(ISMP, Oct 22, 2015)



“Over the last 20 or 25 years, this entire area of study and research has undergone a transformation in the US, withering into near non-existence.” Without ongoing studies, key product information that could promote safer pharmaceutical preparation and reduce the risk of medication errors is becoming quite scarce.

“Pharmacy students, including PharmD candidates, used to be frequent sources of new clinical pharmaceuticals research, especially under the guidance of academic mentors. Unfortunately, few pharmacy schools and their students conduct laboratory research projects anymore.”

Pharmaceuticals

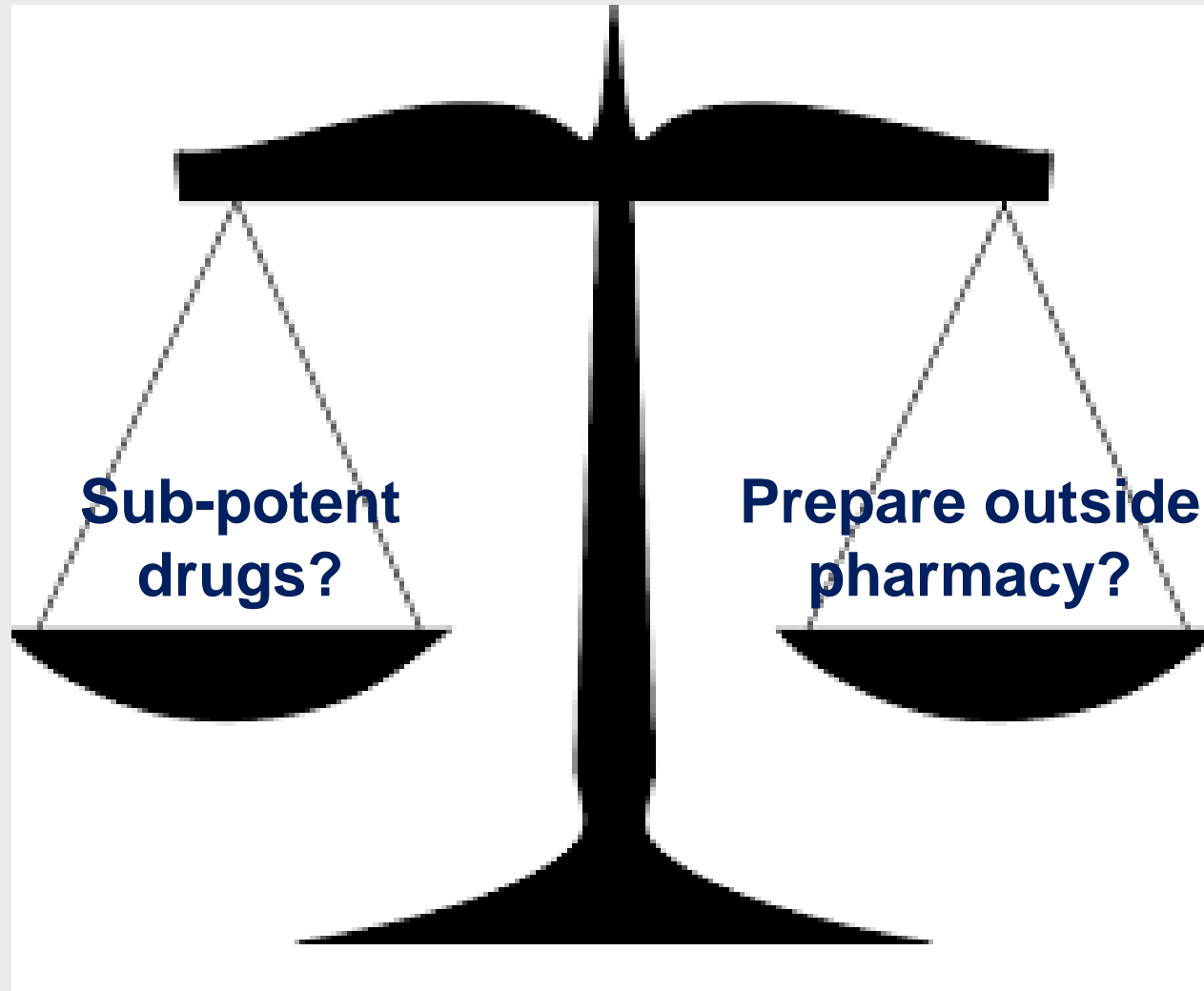
In the last 20 years, there has been more than an 80% decline in new research studies of drug stability, potency, and compatibility.



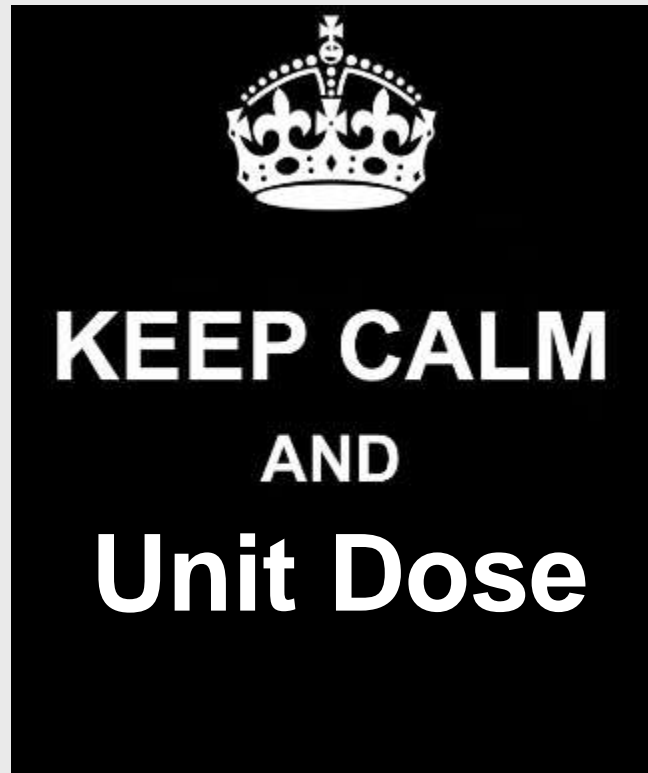
Our Best Advice...

1. Ensure everyone knows the risks
2. Conduct a comprehensive review and risk assessment analysis of the drugs you are currently storing in syringes. If there are high risk agents that you can identify where any loss of concentration could be clinically significant (e.g. antibiotics, chemotherapy, anticonvulsants), prepare medications as close to the administration time as possible.
3. Evaluate what drugs may be packaged in alternate formats e.g. minibags.
4. Purchase commercially available products approved for use in Canada
5. If you are preparing drugs to be stored in syringes do not use syringes from the affected lots of BD syringes.

Balance Risk vs. Benefit?



Don't Abandon BEST PRACTICE!



But....

What else?

Curriculum Redesign ??

The pharmacy profession is responsible and accountable to society for the rational and safe use of medicines. Ideally, pharmacy practitioners have the breadth of knowledge, skills, and attitudes necessary to provide high quality healthcare in all its dimensions.

(CSHP. Education: Statement on Collaborative Development, Delivery, and Evaluation of Pharmacy Curricula; 2011)

Evolution of Pharmacist Practice

- Over the last decades, focus of pharmacists activities has shifted from compounding and distribution to provision of direct patient care
- The by-product of this change is that compounding has increasingly been left behind and academic curricula have essentially eliminated this from their pharmacy programs.
- New pharmacists generally do not have compounding skills unless they have gained special extra-curricular training.
- Pharmacist Technicians roles and curriculum have also expanded.

(Thiessen, 2013)

The GAP



Lawrence A. Trissel

“Whose job is it to **protect patients from harm** from drug instabilities and incompatibilities and other aspects of clinical pharmaceuticals? Nurses and physicians? Not likely. Drug companies or the FDA? Even less likely.

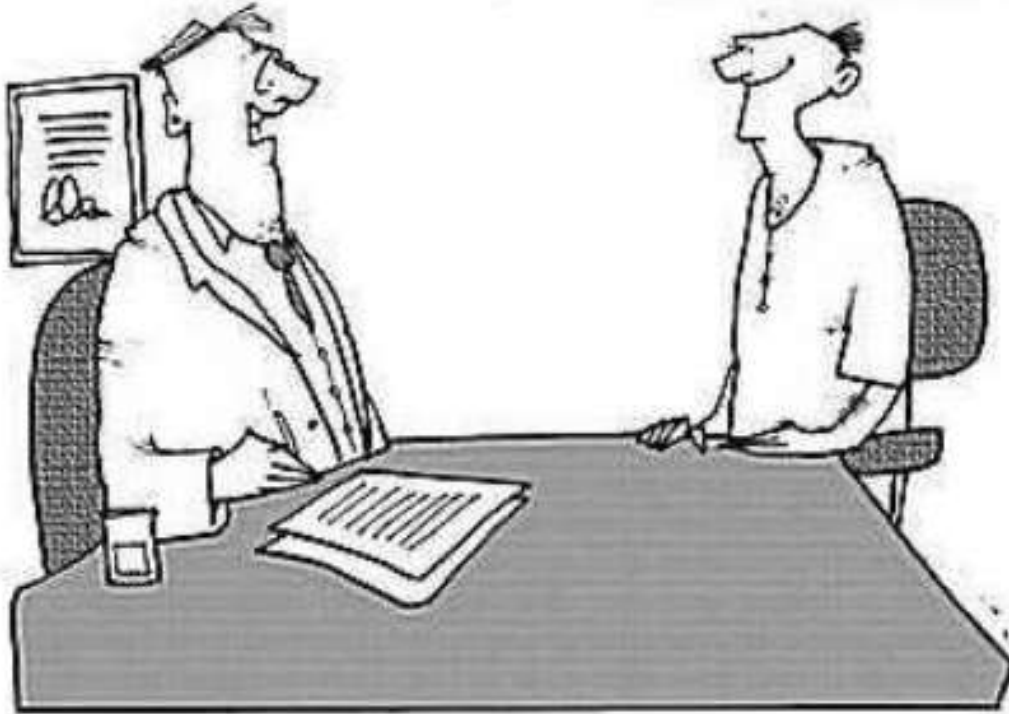
If not pharmacists, the self-declared drug experts, then who? If the pharmacy profession in the US abandons it, what does that say about pharmacy schools, pharmacy professional institutions and associations, and pharmacy practitioners?”

CSHP Statement

CSHP advocates that the community of pharmacist practitioners work with educational institutions, accreditors of educational programs, and regulatory authorities to collaboratively develop, deliver, and evaluate pharmacy educational curricula designed to prepare pharmacy practitioners to meet the medication-related needs of society.

(CSHP. Education: Information Paper on Collaborative Development, Delivery, and Evaluation Pharmacy Curricula; 2011)

Incident Management ???



There's a drug shortage. I'm thinking of replacing your meds with eight hugs a day before & after meals!

Unfortunately, Practice doesn't always mean perfect



References

Thiessen, J. A review of the Oncology Under-Dosing Incident; 2013

CSHP. Education: Information Paper on Collaborative Development, Delivery, and Evaluation Pharmacy Curricula; 2011

CSHP. Education: Statement on Collaborative Development, Delivery, and Evaluation of Pharmacy Curricula; 2011