2018
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OF COMPOUNDING

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REGULATORY PANEL LANDSCAPE

UNITED STATES – CANADA – EUROPE

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HOUSEKEEPING

Cell Phones

Download the Slides

Questions

No photography, audio, or video recordings

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DISCLAIMER

DISCLAIMER: The information contained in this program, which may include treatment modalities, diagnostic and therapeutic information, and instructions related to regulatory guidelines and current standards of practice for pharmacy compounding, is FOR EDUCATIONAL PURPOSES ONLY and should not be taken as a treatment regimen, product indication, suggested treatment modality, or suggested standard of practice. NOTE TO MEDICAL OR ALLIED HEALTH PROFESSIONAL: Any treatments, therapies, or standards of practice must be fully investigated and prescribed by a duly licensed medical practitioner in accordance with accepted professional standards and compendia. Any regulatory or practice standard must be fully investigated by a licensed pharmacist in accordance with accepted professional practice standards and compendia.

QUINTON DIDYK, BSc, BS Pharm, RPEBC

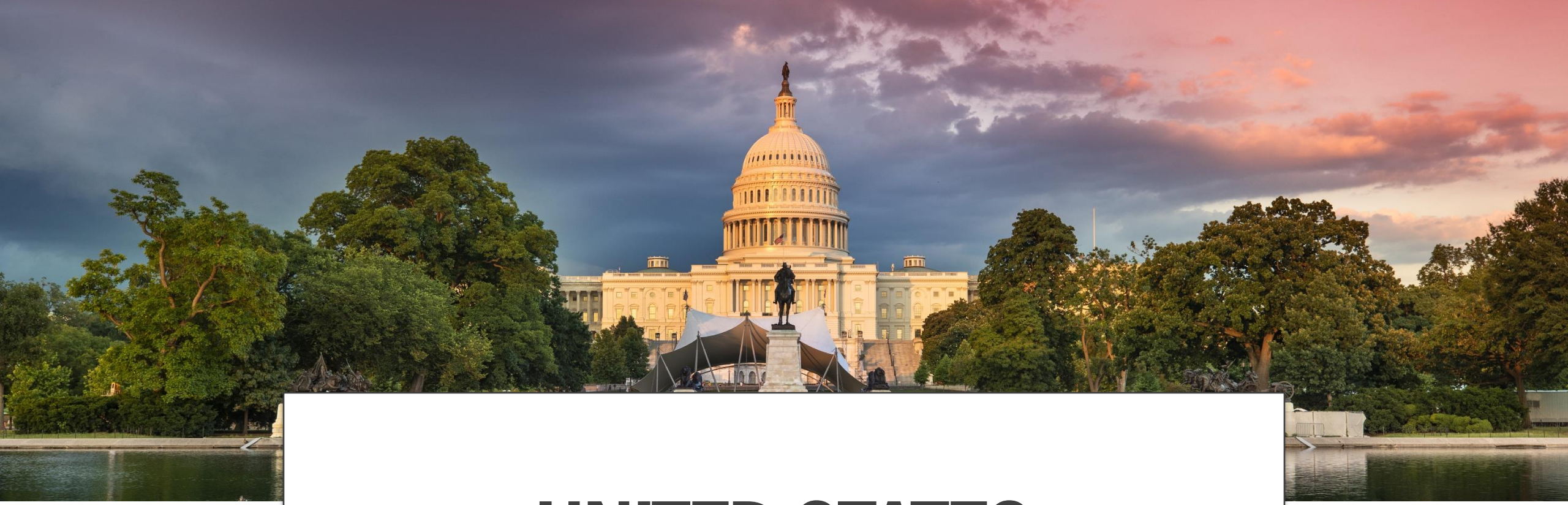
- Graduated in 2002 from the University of Manitoba Faculty of Pharmacy
- Experienced in community health services and pharmacy practice
- Received the Young Leader in Pharmacy Award n 2006, from the Manitoba Society of Pharmacists
- Has been a facilitator for sterile and non-sterile compounding programs since 2008
- Owns and operates the largest compounding-only facility in Manitoba that delivers specialized care on a daily basis
- Became a surveyor for the Accreditation Commission for Health Care (ACHC) in 2015

HANNEKE LATER-NIJLAND, PharmD, PhD, LLM

- Lawyer and pharmacist
- PhD, Clinical Pharmacokinetics
- Former inspector for Clinical Trials and Pharmacovigilance at the Netherlands Inspectorate for Healthcare (IGZ)
- Lecturer, Leiden University (Netherlands)
- Areas of expertise: marketing authorizations, reimbursement, compliance, pharmacovigilance, clinical trials, compounding and advertising issues, product liability issues, intellectual properly and regulatory issues

AARON LOPEZ, JD, FCLS

- Has more than 20 years of experience working with clients in multiple industries to provide insight and a voice in legislative and political processes at the international, federal, and state levels.
- Provides issue management and crisis management capability for clients.
- Has built strong working relationships with the FDA, DOT, USDA, EPA, DOD, The White House, The House of Representatives, and the U.S. Senate.
- Has worked closely with the European Union Commissioners and regulators in Europe.
- developed and executed successful strategies to rebuild public trust and develop positive government relations.



UNITED STATES

COMPOUNDING ENVIRONMENT

- Reasons why it is the best profession
- Perception of the industry
- Growth potential

FOOD AND DRUG ADMINISTRATION (FDA)

- 503A – Traditional Pharmacies
- 503B – Outsourcing Facilities
- Pharmacy Compounding Advisory Committee
- Guidance Documents
  - Insanitary Conditions
- Global Reach

UNITED STATES PHARMACOPEIA (USP)

- 795 – Non-Sterile Compounding
- 797 – Sterile Compounding
- 800 – Hazardous Drugs
- Other Applicable Sections

STATE BOARDS OF PHARMACY

- Oversight of pharmacy license
- Inspections
- Interactions between Boards and Pharmacies

CANADA

NAPRA

- National Association of Pharmacy Regulatory Authorities

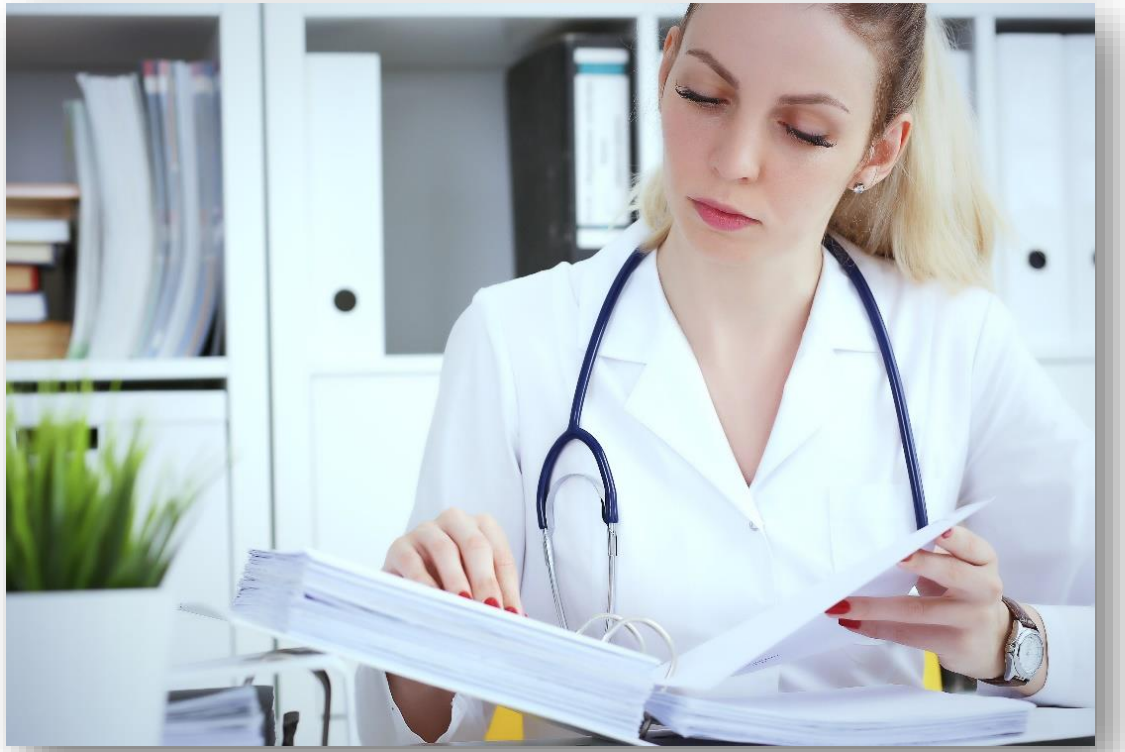
- Canada’s voluntary association of provincial and territorial pharmacy regulatory bodies and the Canadian Forces Pharmacy Services

NAPRA

- Formed in 1995 to provide members a national approach to addressing issues in the practice of pharmacy

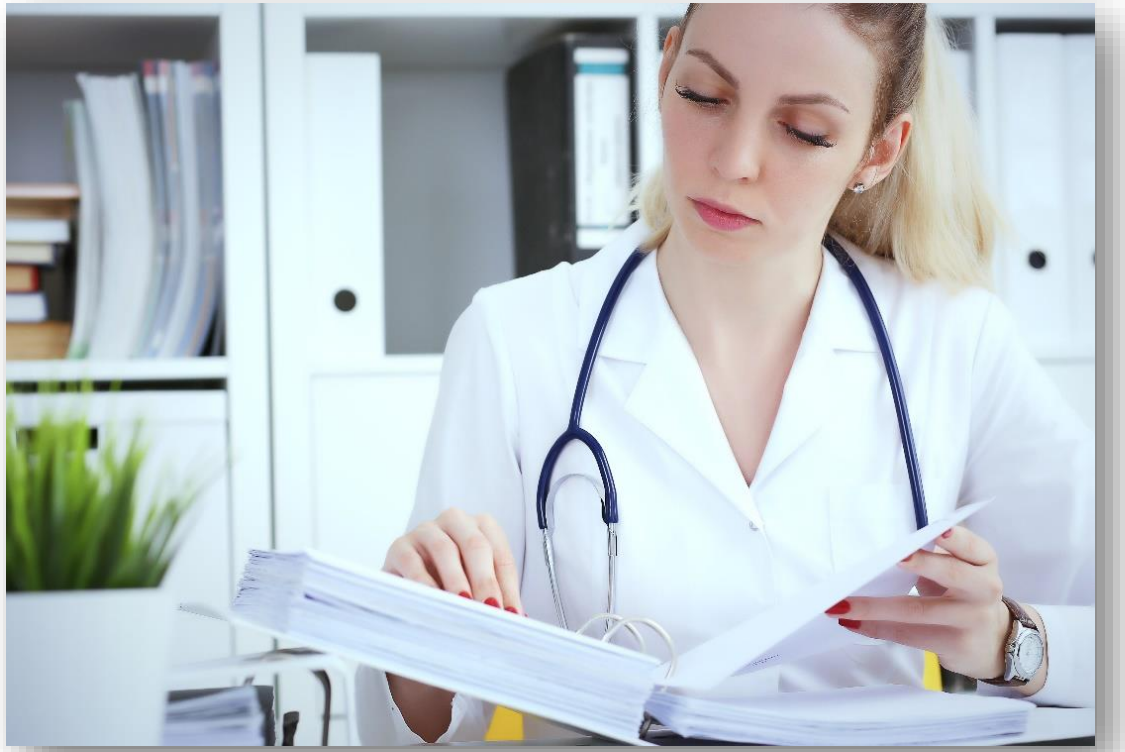
MODEL STANDARDS FOR PHARMACY COMPOUNDING

- Recently released three updated Guidelines to Pharmacy Compounding
  - Previous edition was in 2006



MODEL STANDARDS FOR PHARMACY COMPOUNDING

- Model Standards for Pharmacy Compounding
  - 2014 – Non-hazardous Sterile Preparations
  - 2015 – Hazardous Sterile Preparations
  - 2018 – Non-Sterile Preparations
    - Accompanied by a Guidance Document
- Heavily reference USP <795> and <797>, published in 2013



NAPRA

- No direct regulatory function
- Provinces and territories have no requirement to adopt the developed standards
- Each jurisdiction decides
  - Which standards to adopt
  - What timeline they chose for implementation

FEDERAL AND PROVINCIAL IMPLEMENTATION

- Utilizing a multiple-tiered phased approach
  - Policy and procedures
  - Personnel training assessment
  - Quality assurance measures
  - Minimal facility requirements for compounding

CURRENT COMPOUNDING LANDSCAPE

- Most significant changes in practice standards
- Pharmacists are encountering common issues as they strive to comply with NAPRA standards
- Primary challenge is the allocation of financial and human resources
- Requires dedication by all personnel involved

EUROPE

DISCLOSURES

WIDELY RESPECTED
~ LIFE SCIENCES BOUTIQUE ~
CHAMBERS EUROPE 2018

AXON
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health
food
technology

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DEFINITION

- No single definition, not even a single term:
  - Magistral and officinal preparation (*formula magistralis, formula officinalis*)
  - Extemporaneous compounding
  - Individually non-standardised preparations
  - Etc.

EU LEGAL SITUATION FOR COMPOUNDING

- No legal harmonization on European level, outside the scope of **Directive 2001/83/EC.** No binding regulation on European level.
  - European legislation (Directive 2001/83/EC) requests manufacturing authorization and marketing authorization for bringing medicinal products onto the market but exempts compounding:
  - Article 3 Directive 2001/83/EC: Directive does not apply to any medicinal product prepared (1) in a pharmacy in accordance with a medical prescription for an individual patient or (2) in a pharmacy in accordance with the prescriptions of a pharmacopoeia and supplied directly to patients of the pharmacy.
  - Article 40 (2) Directive 2001/83/EC: Manufacture authorization is not required for certain activities where these are carried out for retail supply by pharmacists in dispensing pharmacies.
- Further regulation on Member State level in accordance with **Resolution CM/Res(2016)**

RESOLUTION CM/Res (2016)1

- **Subject:** Quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients

- Not legally binding.

- Main points:
  - Pharmacy preparations are not advisable if a suitable pharmaceutical equivalent with a marketing authorisation is available
  - Risk assessment before preparation
  - Good Manufacturing Practice (GMP) Guidelines for high-risk preparations and PIC/S GPP Guidelines for low-risk preparations
  - Product dossier
  - Criteria for a marketing authorisation
  - Compliance with pharmacopoeial requirements

EUROPEAN CASE LAW

- **The Abcur Case**
  - Exception of Art. 3 Directive 2001/83/EC should be interpreted strictly and the conditions are cumulative. The medical prescription must be issued and individual patient must be identified before the preparation of the medicine.
  - Industrially prepared or manufactured by a method involving an industrial process demarcates the partition of the scope of the directive and the exception.
  - This is characterised in general by the standardised production of significant quantities of a medicinal product to be stocked and sold wholesale and the large-scale or serial production of *magistral formulae* in batches.

EUROPEAN CASE LAW

- **The Hecht Pharma Case:**
  - Exception in German Marketing of Medicine Law for preparation of up to 100 packages a day is compliant with the European exception.
- **Conclusion of AG Novartis Case:**
  - Repackaging in a pharmacy is not considered as falling under the scope of the *formula magistralis* exception. Decision to be awaited.

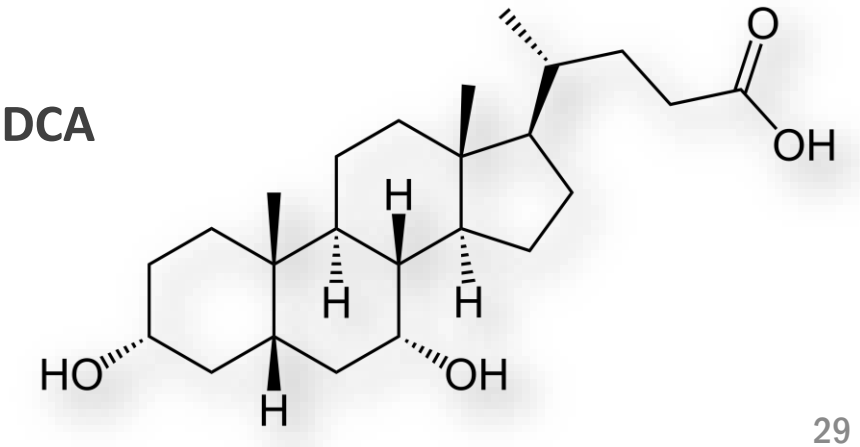
DUTCH SITUATION

- Dutch Medicines Act
  - **Art. 18 par. 5:** *"not prohibited to prepare medicine without a license on a small scale if it is done for the purpose of direct dispensing at a pharmacy."*
  - **Art. 40 par. 3 sub a:** *"not prohibited to place medicine on the market on a small scale if it is done for the purpose of direct delivery at a pharmacy."*

- Decree Medicine Act:
  - **Art. 2:** Medicines prepared in a pharmacy (…) will only be dispensed when compliant with the standards of a Pharmacopoeia (European, if not available: national, U.S. or Japanese). Only sound components will be used for the preparation.

AMC COMPOUNDING CDCA

- **April 2018:** AMC starts compounding **chenodeoxycholic acid (CDCA)** for 50 patients with **cerebrotendinous xanthomatosis (CTX)**
- **April 2018:** The Dutch government seems pro-compounding, sees it as a tool to lower drug prices and expresses its support and confirms 50 patients qualifies as a small scale
- **May 2018:** Manufacturer of **CDCA**, Leadiant Biosciences, requests enforcement by Inspectorate for Healthcare
- Dutch Health Institute concludes used raw materials are not compliant with European Pharmacopoeia standards
- **August 2018:** AMC stops manufacturing and recalls compounded **CDCA**



REIMBURSEMENT

- Not arranged on a European level (outside of EUNetHa initiatives)
- **Netherlands**
  - As per 1 January 2019, compounded products may be charged, even if it concerns a prescribed Rx medicinal product (which has obtained a marketing authorization)
  - This also concerns 'special' compounding, *e.g.* when aseptic preparation, or working with hazardous materials is required, although from the view point of quality and efficiency, such compounding should take place in specialized pharmacies
  - However, whether the product is compounded by a dispensing care provider or by a compounding care provider on an individual prescription, the compounded quantity must correspond with the quantity needed to dispense the Rx medicinal product based on the individual prescription
- Unprecedented trends are being perceived in certain MS

DRUG SHORTAGES RECURRING ISSUE

- Start 2018, a new Dutch law was enacted, allowing the Inspectorate to decide that in order to cover up for drug shortages in ‘special needs’ cases, a medicinal product may be dispensed by a manufacturer, a wholesaler or a pharmacist to a medical doctor

- Remarkable as:
  1. Does this comply with European legislation?
  2. This could entail a compounding exemption on a large-scale and
  3. The rationale for this provision, being the shortages, are not mentioned in the provision itself.
  4. A legislative proposal has been drafted setting pharmacists free from patent infringement when compounding for direct use, individual cases, on medical prescription. (timing ~ Unified Patent Court)

INDUCED COMPETITION

- The Dutch government now seems to induce competition between industrially prepared approved medicinal products and compounded products in order to restrain the costs of medicinal products

- Court of Justice of the EU **(CJEU)** C-185/10 Commission v. Poland:
  - *"(…) inasmuch that statutory provision dispenses with the requirement for a marketing authorization **(MA)** for medicinal products from abroad which have*
  - *the same active substances;*
  - *the same dosage, and*
  - *the same form*
  - *as those having obtained a MA in Poland, on condition that the price of those imported medicinal products is competitive in relation to the price of the products having obtained such MA, (…) Poland has failed to fulfil its obligations under article 6 of the Medicines Directive (Dir 2001/83/EC, as amended)"*

PROHIBITIONS IN ADVERTISING

- Prohibition advertising (unauthorized) Rx medicinal products
  - It is prohibited to advertise compounded Rx products
  - It is allowed to *inform* about the compounded product (NL)
  - It is allowed to advertise the *service* of compounding (NL)

QUESTIONS?