HOUSE OF REPRESENTATIVES STAFF ANALYSIS

BILL #: PCB HCC 08-15 Drugs, Devices and Cosmetics
SPONSOR(S): Healthcare Council
TIED BILLS: **IDEN./SIM. BILLS:**

REFERENCE	ACTION	ANALYST	STAFF DIRECTOR
Orig. Comm.: Healthcare Council		Lowell/Massengale	Gormley
1)			
2)			
3)			
4)			
5)			

SUMMARY ANALYSIS

The Proposed Council Bill significantly reorganizes Part I of Chapter 499 by combining relevant sections of law together, including sections relating to enforcement and rule authority, generally-applicable definitions, and criminal prohibitions.

The bill clarifies several requirements under current law relating to distribution and authentication of pedigree papers. In addition, the bill expands the definition of manufacturer to clarify that the manufacturing process is not subject to the pedigree papers requirement.

The bill amends the limited prescription drug veterinary wholesale distributor permit to prohibit the permittee from distributing, rather than prohibit the permittee from "being permitted to distribute", prescription drugs for human use to any person who is authorized to sell, distribute, purchase, trade, or use these drugs on or for humans.

Finally, the bill expands the ability of prescription drug wholesale distributors to use the direct-purchase pedigree paper by increasing the number of allowed intracompany transfers from one transfer to "one or more transfers".

The bill appears to have an insignificant fiscal impact on the Drug, Device and Cosmetic Trust Fund (see fiscal analysis.)

The bill will take effect July 1, 2008.

FULL ANALYSIS

I. SUBSTANTIVE ANALYSIS

A. HOUSE PRINCIPLES ANALYSIS:

Provide limited government – the bill expands the ability of prescription drug wholesale distributors to use the less-burdensome direct-purchase pedigree paper.

B. EFFECT OF PROPOSED CHANGES:

Current Situation

Regulation of Drugs, Devices, and Cosmetics

Part I of Chapter 499 (chapter) requires the Department of Health (department) to regulate drugs, devices, and cosmetics. Among many other provisions, the chapter provides for:

- Criminal prohibitions against the distribution of contraband and adulterated prescription drugs.
- Regulation of the advertising and labeling of drugs, devices, and cosmetics.
- Establishment of permits for manufacturing and distributing drugs, devices, and cosmetics.
- Regulation of the wholesale distribution of prescription drugs, which includes pedigree papers.
- Regulation of the provision of drug samples.
- Establishment of the Cancer Drug Donation Program.
- Establishment of numerous enforcement avenues for the Department of Health, including seizure and condemnation of drugs, devices, and cosmetics.

The chapter has been amended numerous times over the past two decades. As a result, the chapter has become fractured:

- The Department of Health's general administrative and enforcement authority is spread over five separate sections of law.[1]
- Criminal prohibitions are spread over six sections of law.[2]
- Permit definitions are spread over five sections of law.[3]
- Generally applicable definitions are spread over five sections of law.[4]
- The terms "legend drug", "prescription drug" and "medicinal drug" are used interchangeably to refer to prescription drugs regulated by the Federal Food, Drug, and Cosmetic Act.[5]
- The terms "wholesaler", "wholesale distributor", and "wholesale drug distributor" are used interchangeably to refer to a person who engages in the wholesale distribution of prescription drugs.[6]

In addition, there are numerous errors in the chapter, such as apparent inconsistent provisions and incorrect cross-references.[7]

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[1] Sections 499.004, 499.0053, 499.07, 499.071, and 499.081, F.S.
[2] Sections 499.0051, 499.0052, 499.00535, 499.00545, 499.069, and 499.0691, F.S.
[3] Sections 499.012, 499.0122, 499.013, 499.014, and 499.028, F.S.
[4] Sections 499.003, 499.012, 499.0121, 499.029, and 499.0661, F.S.
[5] *See, e.g.,* s. 499.006 (using the terms "legend drug" and "prescription drug"). *See also* s. 499.003(25), F.S. (defining "legend drug", "prescription drug", and "medicinal drug" identically).
[6] *See, e.g.,* ss. 499.012(8)(b), F.S. (using the term "wholesale drug distributor") and 499.0121, F.S. (using the terms "wholesaler" and "wholesale drug distributor").

Pedigree Papers

The prescription drug wholesale distribution market, nationwide, is generally operated by three major companies: AmerisourceBergen Corp., Cardinal Health Inc., and McKesson Corp.[8] Together, these companies hold anywhere from 90 to 95 percent of the prescription drug wholesale distribution market.[9] In addition to these primary wholesale distributors, there are a number of secondary wholesale distributors who may serve a smaller or specialized market, such as distributing directly to individual physician offices. In Florida, there are approximately 360 in-state and out-of-state prescription drug wholesale distributors (permittees).[10] The number of permittees has declined approximately 75 percent since 2003, illustrating a considerable consolidation over the past several years. This consolidation is likely due in part to more stringent permit application requirements enacted in 2003 by the Legislature.[11]

The pedigree paper requirement is a key tool used to regulate these prescription drug wholesale distributors. A pedigree paper is a document that records the distribution of a prescription drug, from initial sale by a manufacturer, to sale by one or more wholesale distributors, to final sale to a person administering or dispensing the prescription drug. The purpose of the pedigree paper is to document prior sales in order to increase the safety of the prescription drug supply chain by preventing the introduction of counterfeited or diverted prescription drugs.

Pedigree Papers—Federal

At the federal level, the pedigree paper must be provided by each person engaged in the wholesale distribution of a prescription drug who is not an authorized distributor of record for the prescription drug.[12] This requirement does not explicitly preempt state regulation, but serves as a minimum requirement for wholesale distributors. The pedigree paper must identify each prior sale, purchase, or trade of the prescription drug and must be provided for each wholesale distribution, including distributions to authorized distributors of record and retail pharmacies.[13] Under the final regulations promulgated by the United States Food and Drug Administration (FDA), the pedigree paper must include the following information:

- The proprietary and established name of the drug;
- Dosage;
- Container size;
- Number of containers;
- The drug's lot or control number;
- The business name and address of all parties to each prior transaction involving the drug, starting with the manufacturer; and
- The date of each previous transaction.[14]

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[7] *See., e.g.*, s. 499.05, F.S. (incorrectly referencing s. 499.006, F.S., instead of s. 499.066, F.S.) and ss. 499.003(4), F.S. (requiring authentication of a pedigree paper upon distribution of the drugs) and 499.0121(4), F.S. (requiring authentication of a pedigree paper upon receipt of the drugs).

[8] *See* http://www.marketwatch.com/news/story/growing-share-big-three-drug/story.aspx?guid=%7B9F3862C1-7E3A-4D82-94B7-A8E4AE5DAE6A%7D (last updated May 30, 2007).

[9] *Id.*

[10] *See* Department of Health, Medical Quality Assurance Annual Report: July 1, 2006 – June 30, 2007.

[11] CS/CS/SB 2312; Chapter 2003-155, L.O.F.

[12] An "authorized distributor of record" or "ADR" is a wholesale distributor with whom the manufacturer has an ongoing business relationship to distribute the manufacturer's products.

[13] Pub. L. No. 102-353, §4 (1992); 21 U.S.C. §353(e) (2000) (commonly referred to as the Prescription Drug Amendments, or PDA).

[14] 21 C.F.R. §203.50(a) (2007).

There are two significant exceptions to the federal pedigree paper requirement. The first, noted above, is for authorized distributors of record. The second is for "intracompany transfers", a term which is not defined in federal law.

Shortly before the December 1, 2006, effective date of the final regulations, however, the United States District Court for the Eastern District of New York issued a preliminary injunction enjoining the enforcement of a portion of the final regulations that specified the information required to be included on the pedigree (described above).[15]

Pedigree Papers—Florida

In Florida, the pedigree paper must be provided by each person engaged in the wholesale distribution of a prescription drug. A wholesale distributor who receives a pedigree paper must authenticate it by verifying that each transaction listed on the pedigree paper has occurred.

There are two forms of the pedigree paper. The first form is known informally as the "direct purchase" pedigree paper because a wholesale distributor must generally purchase the prescription drug directly from the manufacturer and subsequently directly distribute the prescription drug (with an intracompany transfer) to an end user or a chain pharmacy warehouse. The second form of pedigree paper must be used for all other wholesale distributions. The differences between the two forms of the pedigree paper is illustrated in the table below.

Full Pedigree	Direct Purchase Pedigree
No.	Statement, under oath, that "This wholesale distributor purchased the specific unit of the prescription drug directly from the manufacturer."
Name of the prescription drug as it appears on the label.	**Same.**
Quantity, dosage form, and strength of the prescription drug.	**Same.**
Lot numbers of the prescription drug.	*Maintained by the wholesale distributor, made available to the department upon request.*
Name and address of each owner of the prescription drug and his or her signature.	Name and address of the wholesaler and the purchaser of the prescription drug.
Shipping information, including name and address of each person certifying delivery or receipt of the prescription drug.	*Maintained by the wholesale distributor, made available to the department upon request:* The point of origin of the prescription drugs, including intracompany transfers, and the date of the shipment from the manufacturer to the wholesale distributor.
Invoice number, shipping document number, or another number uniquely identifying the transaction.	*Maintained by the wholesale distributor, made available to the department upon request:* Invoice numbers from the manufacturer.
Certification that recipient wholesale distributor has authenticated pedigree papers.	**No.**

[15] *RxUSA Wholesale, Inc. v. Department of Health and Human* Services, 467 F.Supp.2d 285 (E.D.N.Y. 2006).

Full Pedigree	Direct Purchase Pedigree
The unique serial of the specific unit of prescription drug, if the manufacturer or repackager has uniquely serialized the individual prescription drug unit.	**No.**
Name, address, telephone number and, if available, e-mail contact information of each wholesale distributor involved in the chain of the prescription drug's custody.	**No.**

Florida law provides several exceptions to the pedigree paper requirement, including:

- The wholesale distribution of compressed medical gas.
- The wholesale distribution of veterinary prescription drugs.
- Drop shipments of prescription drugs by prescription drug manufacturers.[16]
- Certain distributions of prescription drugs by wholesale distributors within an affiliated group.[17]

Limited Veterinary Prescription Drug Wholesaler

A number of drugs intended solely for animals are required by federal law to be prescribed by a licensed veterinarian.[18] In addition, certain drugs intended for human use are frequently prescribed for animal use, such as the antibiotic amoxicillin.

In Florida, a wholesale distributor who only distributes veterinary prescription drugs must obtain a veterinary prescription drug wholesaler permit. However, prior to 2006, if a veterinary prescription drug wholesale distributor sought to distribute human and animal prescription drugs to veterinarians, the distributor would have been required to obtain a prescription drug wholesaler permit.[19] The prescription drug wholesaler permit requires a $100,000 security bond and an extensive permit application.

In 2006, the Legislature created a new permit called a "limited prescription drug veterinary wholesaler permit."[20] The new permit authorizes the wholesale distributor to distribute human and animal prescription drugs to certain persons. However, the wholesale distributor is limited to distributing human prescription drugs worth no more than 30 percent of the wholesaler's total annual prescription drug sales.[21] Of particular note are two additional requirements:

- The wholesaler must not be permitted, licensed, or otherwise authorized in any state to wholesale human prescription drugs to any person who is authorized to sell, distribute, purchase, trade, or use these drugs on or for humans; and

[16] A "drop shipment" occurs when a wholesale distributor arranges for the direct shipment of a prescription drug from the manufacturer to an end user, such as a hospital, health care practitioner, or pharmacy. Drop shipments are used in a number of situations, such as for prescription drugs with unusual temperature or handling requirements that are not suitable for distribution by a wholesale distributor.

[17] An affiliated group is defined by s. 1504 of the Internal Revenue Code of 1986, as amended, (essentially, one or more companies connected through controlling stock ownership) and must be composed of chain drug entities, including at least 50 retail pharmacies, warehouses, or repackagers, which are members of the same affiliated group

[18] 21 U.S.C. 353(f) (2005).

[19] *See* s. 499.012(g), F.S. (2005) (stating that "a veterinary prescription drug wholesaler that also distributes prescription drugs subject to, defined by, or described by s. 503(b) of the Federal Food, Drug, and Cosmetic Act which it did not manufacture must obtain a permit as a prescription drug wholesaler or out-of-state prescription drug wholesaler in lieu of the veterinary prescription drug wholesaler permit").

[20] *See* s. 499.012(h), F.S. (2007).

[21] *Id.*

- The wholesaler must maintain at all times a license or permit to engage in the wholesale distribution of prescription drugs in compliance with laws of the state in which it is a resident.

As no other state has created a license that authorizes a veterinary wholesale distributor to distribute human drugs for animal use only, an out-of-state wholesaler cannot both be licensed to engage in wholesale distribution of prescription drugs and not be licensed to engage in the wholesale distribution of prescription drugs to a person who sell, distribute, purchase, trade, or use these drugs on or for humans.

According to the Department of Health, 18 out-of-state wholesale distributors have applied for the limited prescription drug veterinary wholesaler permit. Of these applicants, none have been approved because of the inconsistency noted above.

Medical Convenience Kits

According to the FDA, medical convenience kits:

> "contain devices and prescription drugs that are combination products under 21 CFR §3.2(e)(2), which are defined as "two or more separate products packaged together in a single package or as a unit and comprised of a drug and device products, device and biological products, or biological and drug products."[22]

Medical convenience kits are generally sterilized and sealed; thus, opening the kit during the distribution process destroys the value of the kit.

The FDA has stated that the prescription drug within a convenience kit is separable and subject to the federal pedigree requirement, even though the outside of the sealed kit may be labeled with a lot number that is different than the lot number of prescription drug within the kit. Florida law does not specifically address whether a wholesale distributor must open the kit to verify the product inside is the same product on the pedigree paper.

Effect of Proposed Changes

The bill significantly reorganizes Part I of Chapter 499 (chapter) by consolidating:

- The Department of Health's enforcement and rule authority.[23]
- Criminal prohibitions.[24]
- Permit definitions and requirements.[25]
- Generally applicable definitions.[26]
- The use of the terms "legend drug", "prescription drug" and "medicinal drug" in favor of "prescription drug."
- The use of the terms "wholesaler", "wholesale distributor", and "wholesale drug distributor" in favor of "wholesale distributor."

The bill also clarifies that:

[22] United States Food and Drug Administration, Guidance for Industry, Prescription Drug Marketing Act (PDMA) Requirements, Questions and Answers (2006).
[23] Sections 499.004, 499.0053, 499.07, 499.071, and 499.081, F.S. are transferred and renumbered in s. 499.002, F.S.
[24] Sections 499.0052, 499.00535, 499.00545, 499.069, and 499.0691, F.S. are transferred and renumbered in s. 499.0051, F.S.
[25] Sections 499.0122, 499.013, 499.014, and 499.028, F.S. are transferred and renumbered in s. 499.012, F.S.
[26] Sections 499.012, 499.0121, 499.029, and 499.0661, F.S. are transferred and renumbered in s. 499.003, F.S.

- A wholesale distributor may authenticate a sealed medical convenience kit without physically opening the kit.
- A pedigree paper must be authenticated upon receipt, rather than upon distribution.
- A pedigree paper must be provided prior to, or simultaneous with, the distribution of the prescription drug, rather than only prior to distribution.

The bill expands the definition of manufacturer to include holder or holders of a New Drug Application (NDA), an Abbreviated New Drug Application (ANDA), a Biologics License Application (BLA), or a New Animal Drug Application (NADA), provided that such application has become effective or is otherwise approved consistent with s. 499.023; a private label distributor for whom the private label distributor's prescription drugs are originally manufactured and labeled for the distributor and have not been repackaged; or the distribution point for the manufacturer, contract manufacturer or private label distributor whether the establishment is a member of the manufacturer's affiliated group or is a contract distribution site. The expansion of the definition will ensure that the process of manufacturing a prescription drug is exempt from the pedigree papers requirement.

The bill addresses the conflict within limited prescription drug veterinary wholesale distributor permit by prohibiting the permittee from distributing, rather than prohibiting the permittee from "being permitted to distribute", prescription drugs for human use to any person who is authorized to sell, distribute, purchase, trade, or use these drugs on or for humans

Finally, the bill substantially rewrites the pedigree papers requirement, creating a new section of law and organizing the requirement within the following framework:

- Application—specifies who must provide a pedigree paper.
- Format—specifies which pedigree paper must be used and what must be included in it.
- Exceptions—specifies the exceptions to the requirement.

The rewrite does not substantively change the pedigree papers requirement, with one exception. The bill expands the ability of a prescription drug wholesale distributor to use the direct-purchase pedigree paper by increasing the number of allowed intracompany transfers from what appears to be one transfer[27] to "one or more transfers". The term "intracompany" is defined to mean any transaction or transfer between any parent, division, or subsidiary wholly owned by a corporate entity.

C. SECTION DIRECTORY:

Section 1. Amends s. 499.002, F.S., relating to the purpose of Part I of Chapter 499.

Section 2. Amends s. 499.003, F.S., relating to definitions.

Section 3. Amends s. 499.005, F.S., relating to prohibited acts.

Section 4. Amends s. 499.0051, F.S., relating to criminal acts involving contraband or adulterated drugs.

Section 5. Amends s. 499.0054, F.S., relating to advertising and labeling of drugs, devices, and cosmetics.

[27] *See* s. 499.003(31)(b), F.S. (defining the use of the direct-purchase pedigree for distributions from the manufacturer to the wholesale distributor directly to, or through "an" intracompany transfer, the end user).

Section 6. Amends s. 499.006, F.S., relating to adulterated drugs or devices.

Section 7. Amends s. 499.007, F.S., relating to misbranded drugs or devices.

Section 8. Amends s. 499.008, F.S., relating to adulterated cosmetics.

Section 9. Amends s. 499.009, F.S., relating to misbranded cosmetics.

Section 10. Amends s. 499.01, F.S., relating to permits; applications; renewal; and general requirements.

Section 11. Amends s. 499.012, F.S., relating to wholesale distribution; definitions; permits; applications; and general requirements.

Section 12. Amends s. 499.01201, F.S., relating to Agency for Health Care Administration review and use of statute and rule violation or compliance data.

Section 13. Amends s. 499.0121, F.S., relating to storage and handling of prescription drugs and recordkeeping.

Section 14. Creates s. 499.012111, F.S., relating to pedigree papers.

Section 15. Repeals s. 499.0122, F.S., relating to medical oxygen and veterinary legend drug retail establishments.

Section 16. Repeals s. 499.013, F.S., relating to manufacturers and repackagers of drugs, devices, and cosmetics.

Section 17. Amends s. 499.015, F.S., relating to registration of drugs, devices, and cosmetics and issuance of certificates of free sale.

Section 18. Amends s. 499.023, F.S., relating to new drugs; sale, manufacture, repackaging, distribution.

Section 19. Amends s. 499.024, F.S., relating to drug product classification.

Section 20. Amends s. 499.025, F.S., relating to drug products in finished, solid, oral dosage form.

Section 21. Amends s. 499.028, F.S., relating to drug samples or complimentary drugs; starter packs; and permits to distribute.

Section 22. Amends s. 499.029, F.S., relating to the Cancer Drug Donation Program.

Section 23. Amends s. 499.03, F.S., relating to unlawful possession of certain drugs without prescriptions.

Section 24. Amends s. 499.032, F.S., relating to phenylalanine.

Section 25. Amends s. 499.033, F.S., relating to ephedrine.

Section 26. Amends s. 499.035, F.S., relating to dimethyl sulfoxide.

Section 27. Amends s. 499.039, F.S., relating to the sale, distribution, or transfer of harmful chemical substances; penalties; and authority for enforcement.

Section 28. Amends s. 499.04, F.S., relating to fee authority.

Section 29. Amends s. 499.041, F.S., relating to the schedule of fees for drug, device, and cosmetic applications and permits, product registrations, and free-sale certificates.

Section 30. Amends s. 499.05, F.S., relating to rules.

Section 31. Amends s. 499.051, F.S., relating to inspections and investigations.

Section 32. Amends s. 499.052, F.S., relating to records of interstate shipment.

Section 33. Amends s. 499.055, F.S., relating to reports and dissemination of information by department.

Section 34. Amends s. 499.057, F.S., relating to expenses and salaries.

Section 35. Amends s. 499.06, F.S., relating to embargoing, detaining, or destroying article or processing equipment which is in violation of law or rule.

Section 36. Amends s. 499.062, F.S., relating to cause for seizure and condemnation of drugs, devices, or cosmetics.

Section 37. Amends s. 499.065, F.S., relating to imminent danger.

Section 38. Amends s. 499.066, F.S., relating to penalties and remedies.

Section 39. Amends s. 499.0661, F.S., relating to cease and desist orders.

Section 40. Amends s. 499.067, F.S., relating to denial, suspension, or revocation of a permit, certification, or registration.

Section 41. Provides an effective date of July 1, 2008.

II. FISCAL ANALYSIS & ECONOMIC IMPACT STATEMENT

A. FISCAL IMPACT ON STATE GOVERNMENT:

1. Revenues:

   None.

2. Expenditures:

The Department of Health projects that they will need two full-time equivalent positions to verify compliance with the audit trail requirements and to authenticate direct purchase pedigrees for 151 in-state and 197 out-of-state prescription drug wholesalers; resulting in a recurring fiscal impact of $115,766 to the Drug, Device, and Cosmetic Trust Fund.

B. FISCAL IMPACT ON LOCAL GOVERNMENTS:

1. Revenues:

None.

2. Expenditures:

None.

C. DIRECT ECONOMIC IMPACT ON PRIVATE SECTOR:

Wholesale prescription drug distributors may benefit from the increased use of the less-burdensome direct-purchase pedigree paper.

D. FISCAL COMMENTS:

The department has requested two positions to conduct audit compliance for the direct purchase pedigree requirement due to the language in the definition of "normal distribution chain." The definition permits a wholesale distributor to transfer drugs "intracompany" more than once. Currently, a wholesale distributor may only transfer drugs once. The department has voiced their concern that they would have to audit the companies more thoroughly to ensure compliance with this provision. Due to this change, wholesale distributors will likely choose to use one type of pedigree over another (i.e., direct purchase pedigree). Taking this under consideration, the department has not provided information on how the workload would change in processing or verifying the direct purchase pedigree over the full pedigree.

Currently, wholesale distributors are inspected annually. The Drug, Device, and Cosmetic program currently has 9 full-time equivalent employees that perform site inspections. The department could not provide data on the average time required to conduct a site inspection. The department has stated that they will need to continue to conduct the site inspections so that data may be collected and sent to headquarters to be analyzed and audited to verify compliance. However, the department could not provide adequate information on the man-hours that would be required to conduct an audit of 348 wholesale distributors, since they do not currently perform audits. However, in their fiscal analysis they have projected that it will take 1.5 days perform an audit for each location.

Moreover, according to a Health Quality Interim Project, the number of wholesale distributor permittees has declined approximately 75 percent since 2003. Therefore, it is unclear why current staff could not be reassigned to perform an audit function.

Healthcare Council staff believes that the fiscal impact of the bill will be minimal because the net result of the bill does not appear to increase the department's regulatory duties. Even if the department's projection is correct, the Drug, Device, and Cosmetic Trust Fund currently has sufficient revenue to cover the increased expenditure.

III. COMMENTS

A. CONSTITUTIONAL ISSUES:

1. Applicability of Municipality/County Mandates Provision:

This bill does not require counties or municipalities to spend funds or take action requiring the expenditure of funds. This bill does not reduce the percentage of a state tax shared with counties or municipalities. This bill does not reduce the authority that municipalities have to raise revenues.

2. Other:

None.

B. RULE-MAKING AUTHORITY:

No additional rule-making authority is required as a result of this bill.

C. DRAFTING ISSUES OR OTHER COMMENTS:

None.

D. STATEMENT OF THE SPONSOR

IV. AMENDMENTS/COUNCIL SUBSTITUTE CHANGES