INTRODUCTION

Resolution 515-A-18, “Information Regarding Animal Derived Medications,” introduced by the Michigan Delegation and referred by the House of Delegates (HOD) asked:

That our American Medical Association (AMA): (1) Support efforts to improve cultural awareness pertaining to the use of animal-derived medications when considering different prescription options. (2) Encourage the U.S. Food and Drug Administration to make available to the public an easily accessible database that identifies medications containing ingredients derived from animals.

Some chemical products used as inactive excipients for prescription drugs, as well as some active prescription medications and also some surgical implants, dressings, and mesh, are derived from animal sources. The consumption or use of such products may be objectionable to certain religions or based on consumer choice. The objective of this report is to summarize the issue and current evidence related to animal-derived components of medical products.

BACKGROUND

Some religious faiths forbid the consumption or use of certain animals and substances derived from them. Additionally, individuals who adhere to a vegetarian or vegan diet may prefer to avoid animal-derived medical products. Individuals who want to avoid animal-derived substances for religious or cultural reasons may inquire about the origin or source of the ingredients in their medical products for informed decision-making regarding treatment with the product. Frequently, however, the information regarding ingredients or composition in medications is difficult to obtain by physicians, pharmacists, and patients.1

Many pharmaceutical products (both active and inactive ingredients used in capsules, tablets, injections, vaccines, creams) and surgical products (implants, wound dressings, surgical mesh) contain ingredients derived from animal sources. Animal-derived ingredients (ADIs) are used in many medical fields and cover an array of products usually at minimal concentrations.1 However, a substantial percentage of patients and physicians are unaware that some medications and medical products contain animal products;2 one survey indicated that 84% of patients and 70% of physicians were unaware that several medications contain ADIs. Additionally, 70% of physicians thought it was important to inform patients who might object if such medications are prescribed.3 Some authors have even suggested obtaining informed consent before using animal-derived products.1
POLICY AND LAW

The U.S. Pharmacopeial Convention is a private, nongovernmental organization that publishes the United States Pharmacopeia (USP) and the National Formulary (NF) as official compendia, collectively called the USP-NF. The Federal Food, Drug and Cosmetic Act (FFDCA) expressly recognizes the USP quality standards for medicines. Although much of the USP-NF is legally enforceable, the USP chapters numbered above <999> are general information and generally do not contain any mandatory requirements, but can include recommendations that may help a firm meet the requirements of current good manufacturing processes (CGMPs) as defined by the U.S. Food and Drug Administration (FDA).

FDA Guidance regarding CGMP includes recommendations and precautions when manufacturing ADIs to ensure that contamination by pathogenic agents does not occur. No guidance regarding labeling of ADIs could be located. Although the FDA does have a database that provides information on inactive ingredients present in FDA-approved drug products, its main purpose is to aid industry in drug development; once an inactive ingredient is part of the formulation for an approved drug product, it is no longer considered new and may require less extensive review when used again. The database includes no information regarding the source of the ingredient.

USP-NF general chapter <7> “Labeling” details the requirements for the labeling of active ingredients in pharmaceutical products. No discussion of ingredient source is included. It is noted, however, that many monographs have unique labeling requirements that should be used consistently. USP-NF informational chapter <1091> “Labeling of Inactive Ingredients” states that all ingredients should be disclosed for all medications. The information can be found on the package or insert of a prescription drug and on the drug facts label on the outside of the box for over-the-counter drugs. No requirement exists for a manufacturer to declare how an ingredient is sourced. Additionally, the Code of Federal Regulations calls for all ingredients to be listed, but inactive ingredients are exempt from provisions on misbranding, including some that relate to false or misleading labeling.

CULTURAL CONSIDERATIONS

Some religious groups avoid products from certain animals and many patients have strong religious convictions and beliefs. Vegetarians do not consume foods either directly obtained or using products from the slaughter of an animal. Vegans do not consume any foods originating from animals. Several investigators have surveyed worldwide religious leaders for their opinions regarding the acceptability of certain medical products, both medications and surgical implants/dressings/mesh, for their religions. The surveys generally focused on the six largest religions worldwide and reported varied practices. Many Hindus and Sikhs do not approve of the use of bovine- or porcine-derived products and also follow vegetarian diets. Many who practice Islam or Judaism do not accept the use of porcine-derived products. No principle in Buddhism prohibits the use of animal-derived medical products; however, many members of one of the two major branches follow a vegetarian diet. Most Christians, other than those who follow vegetarian or vegan diets, do not have restrictions. Although Jehovah’s Witnesses refuse blood transfusions, all other medical related products and decisions are at the discretion of the patient and physician. Notably, leaders from all surveyed religions stated that the use of animal-derived medical products would be accepted in the absence of any other alternative or in emergency situations. In difficult situations, religious leaders can also be contacted for guidance.
OTHER CONSIDERATIONS

Various communication practices for patient-directed medication information including readability, container labeling (font, format, and organization), information content length, and supplementary medication instructions have been described, but do not address ingredient lists and source. Some authors have suggested that when healthcare professionals listen to patients’ cultural beliefs, actively involve them in medication prescribing decisions, and take their views and preferences into account, adherence is more likely.

Nevertheless, ADI information is inconsistently reported, difficult to obtain, and sometimes incorrect. Also noteworthy is the fact that excipients and inactive ingredients likely differ between branded and generic forms of medications; therefore, knowledge of the ingredients in a particular branded medication will not guarantee knowledge of generic versions. Some drugs, especially those produced in gelatin capsules, may be available in alternative formulations that do not contain ADIs. Literature discussing clinical decision support systems for physicians and drug databases used by pharmacists has not addressed the issue of ADIs and the inclusion of relevant ADI information. If the source of ADIs, or the fact that an ingredient is an ADI, were required labeling for manufacturers, the potential would exist for this information to be included in the datasets used by clinical decision support systems and drug databases downstream.

PROBLEM MEDICAL PRODUCTS

Both active and inactive pharmaceutical ingredients as well as implants, dressings, and mesh used in surgery can contain ADIs. Some of the more common examples of these ADIs are included in discussion below.

Active Ingredients

The following are examples of products that contain an active ingredient derived from an animal source:

- Conjugated estrogens (Premarin) are derived from the urine of pregnant mares.
- Low molecular weight heparin is porcine-derived.
- Corticotropin is obtained from porcine pituitary gland.
- Hyaluronidase is derived from crude extracts of ovine or bovine testicular tissue.
- Pancreatin (also known as pancreatic enzymes, pancrelipase) is bovine derived.

The product information for these medications indicates that they are animal-derived. However, for some, the information is difficult to locate, often only becoming obvious because of a statement in the “allergy” or “contraindications” section (e.g., This medication is contraindicated in patients with sensitivity to proteins of porcine origin.).

Inactive Ingredients

In a recent review, the use of ADIs in the 100 most commonly prescribed medications in primary care in the United Kingdom found that 74 contained at least one of the three most common excipient ADIs used – gelatin, lactose, and magnesium stearate. Of these 74 products, 42 provided no indication of the presence of an ADI, and 2 products incorrectly stated that no animal content was contained in the product.
Gelatin is a generic term for a mixture of purified protein fractions obtained by hydrolysis of animal collagen obtained from bovine or porcine bone, or from bovine, porcine, or fish skin. It is most frequently used in the capsules of medications. Due to the demand for gelatin-free medication, the production of vegetarian capsules made from hypromellose has expanded, and the use of bioreactors utilizing “cellular agriculture” to create purified proteins that are assembled into collagen and then made into gelatin is becoming popular; but animal-derived gelatin is still used commonly.2,21

Lactose is a natural disaccharide present in the milk of most mammals and is traditionally extracted from milk using bovine rennet. Some manufacturers now use a vegetarian process instead of bovine rennet to extract lactose from bovine milk, but this has caused confusion about suitability for those who avoid bovine products.15 Lactose is widely used as a filler and diluent in tablets and capsules and is also used as a diluent in dry-powder inhalations, in the preparation of sugar-coating solutions, and in some injections.2,15

Stearic acid, utilized as magnesium stearate in products, is a fatty acid sourced from rendered bovine, porcine, or ovine fat or produced from vegetable matter. It is primarily used as a lubricant in capsule and tablet manufacture and improves the solubility of some medications. If the source of the magnesium stearate is not indicated on a drug label, whether or not it is an ADI is unknown and difficult to determine.2

Vaccines

Materials used in the production of some vaccines, e.g., excipients or nutritional supplements for cell cultures, are ADIs. These include gelatin, trypsin (usually bovine sourced), and bovine serum or albumin.22 Religious scholars distinguish between the use of ADIs in oral or non-oral medications and have issued rulings or waivers that allow use of non-oral medications containing ADIs, such as vaccines.2 Despite this distinction, reports persist of concern with ADIs in vaccines.15

Surgical Sutures, Implants, Dressings, and Mesh

The use of synthetic and biological products is widespread in surgeries, and the use of a biologic product that is prohibited or is sacred in a surgical setting is a concern.8,10 Sutures used to close wounds or surgical incisions can contain animal-derived ingredients. A recent study confirmed the frequent use of ADIs, such as collagen membrane, collagen gel, fibrin glue, fibrinogen, aprotinin and some types of chitosan culture media and scaffold, in various arthroscopy products.10 Allograft and xenograft mesh products have also been cited as problematic for patients with issues related to the use of ADIs.11 Authors encourage surgeons to know the source of the products they use as well as the basic requirements of their patient’s faith, possibly even gaining informed consent before the use of animal-derived surgical implants.8,11

CURRENT AMA POLICY

No AMA policy addresses this issue.

CONCLUSION

Several medication ingredients, both active and inactive, and surgical products contain ingredients derived from animal sources. Patients may have strong religious convictions and cultural beliefs leading them to object to using medical products with animal-derived ingredients.
It has been documented that physicians may have a hard time determining the origin of ingredients because the information is inconsistently reported, difficult to obtain, and sometimes incorrect. Many times, reading the list of ingredients of a medical product will not clarify if the product contains any animal-derived ingredients or components. Additionally, the products can vary in regard to ADIs based on the manufacturer, and between brand name and generic versions.

Because no requirement exists for a manufacturer to declare how an ingredient is sourced on label information, this information is not present in clinical decision support systems for physicians and drug databases. Including additional information, such as the presence of ADIs and their source, in the ingredients lists on drug labels and in product information would be beneficial because this information could then be included in information systems used by clinicians and would be more accessible to patients.

RECOMMENDATION

The Board of Trustees recommends the following be adopted in lieu of Resolution 515-A-18, and the remainder of the report be filed:

Animal-Derived Ingredients

Our AMA:

1. Urges the U.S. Food and Drug Administration to require manufacturers to include all ingredients and components present in medical products on the product label, including both active and inactive ingredients, and denote any derived from an animal source. (New HOD Policy)

2. Encourages cultural awareness regarding patient preferences associated with medical products containing active or inactive ingredients or components derived from animal sources. (New HOD Policy)

Fiscal Note: Less than $500
REFERENCES

4. 21 U.S.C. ch. 9 § 301.
7. 21 C.F.R. pt. 201