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Hexachlorophene: Ubiquitous Bacteriostat,
Banned But Possibly Still on the Market Shelf

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Hexachlorophene: Ubiquitous Bacteriostat, Banned but Possibly Still on the Market Shelf

by
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Summary

Hexachlorophene, an anti-bacterial agent that gained wide usage in products ranging from mouthwashes to furnace filters, has been restricted to limited use by the Food and Drug Administration. The consumer, however, will still be purchasing products with hexachlorophene in them including products similar to those that have been found to cause injury or death.

A detailed look at the FDA rules explains how this situation has occurred and reviews which products should and should not still be available for sale. The pitfalls of using a simple label examination test for the presence of hexachlorophene are explained.

Hexachlorophene gained widespread usage. However, recently studies showed previously unknown toxic effects which triggered the FDA restrictions. Even newer regulations (November, 1972) have banned all hexachlorophene from products including feminine hygiene sprays, that are used on or near mucous membranes. Banned products have been found on the market shelf. The presence of these products is explained by the limitations of the FDA recall process.

Introduction

The news media has covered the recent deaths attributed to hexachlorophene and the announcements of its restricted use(1,2); yet the details on the restrictions, the reasons for them and the status of the recalls are not generally known. This bulletin has been prepared to give the community a reference to the present status of hexachlorophene (HCP) and its usage in consumer products.

Hexachlorophene (HCP) Use Regulations (3, 21)

1. Baby powders containing more than .75% HCP are to be recalled because their retention on the body is especially dangerous in light of the recent incident in France. (See paragraph 6, Background.)

2. Stocks of other products containing .75% or more HCP now on the shelves are to be withdrawn to prescription dispensing sale. In those locations which do not have pharmacies, these products are to be recalled.

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3. HCP may not be used in any quantity, i.e. not even .1% or less, as a "preservative in any drug and/or cosmetic product, which in normal use may be applied to mucous membranes or which are intended to be used on mucous membranes, e.g. chapsticks, feminine hygiene sprays, (and) rectal ointments" (21). This additional restriction was established after publication by the FDA in the Federal Register on November 4, 1972. The reason for this restriction is the special complaints about the effects on such tissue by HCP; this is covered in more detail in the section on feminine hygiene sprays.

4. Stores may continue to sell products which contain between .1 and .75% HCP without restriction. Products with these formulations will not be restocked from the manufacturer. Many will be reformulated to eliminate HCP or meet the FDA limitations. This change may not be obvious to the customer even after a close inspection of the label. See the section on product labeling.

5. No product may be manufactured or shipped from the manufacturer for over the counter sale which contains more than .1% by weight HCP. The .1% is permitted for use only as a preservative until replacements can be tested. There will be no limit on the sale of these items.

6. Products containing more than .1% HCP may be manufactured for sale by prescription only. The products will have special warnings on the labels and the manufacturer will have to comply with special regulations. These restrictions will not be in complete effect until the end of 1972. The primary reason for the prescription exception is to permit physicians to prescribe products contining HCP in special situations to control infections (especially in hospitals). The doctor will decide if its efficacy in controlling infections outweighs the dangers of its possible toxicity.

7. Items such as shoelaces or exhaust filters, that is products not covered by the Food, Drug, and Cosmetic Act may continue to contain HCP without any new restrictions (4).

8. Products already purchased by customers containing HCP in any quantity are not affected. Cautious consumers might wish to discard some or all of these products.

Hexachlorophene Labeling

Drugs, including those items normally considered cosmetics but claiming some medicinal benefit, must contain the amount and name of the active ingredient on the label (5). This type of product with HCP exceeding FDA limits could be removed from the shelf by the retailer after a simple inspection of the label. Most often, however, the storekeeper has awaited specific directon to remove a product by the wholesaler or franchise central office. Therefore consumers could check products classified as drugs (although sold without prescription) for HCP, by simply checking the label. That is, pHisoHex Skin Cleanser or the formulation of J & J's First Aid Cream which contained HCP can easily be detected by checking the label. These products may be now reformulated to eliminate HCP - as may all other products which contain HCP - and then be legitimately sold. For the reformulated product, HCP content would not be on the label since it is no longer present. That is, for products of obvious medicinal benefit, if the contents part of the label does not specifically say that HCP is present, then the consumer can legitimately assume that there is no HCP in the package.

However, cosmetics which make no medical claim do not have to list either the active ingredients or the percentage of the active agent (4). While a change in the law has been proposed but not yet enacted - primarily because of the opposition of manufacturers who wish to protect proprietary formulations - the FDA has gotten some manufacturers to voluntarily list the active ingredients, but not the amount, on the label. Whether or not HCP is listed on the label, the retailer finds out that the product must be removed when he is told so by the wholesaler or the manufacturers' representative. The only way the consumer can be assured that HCP is not in a product classified as cosmetics is a) if the manufacturer has stated on the label, because of the HCP scare, that it does not contain HCP, b) if the consumer recognizes a product formerly labeled as containing HCP (voluntarily listed by the manufacturer) and sees that HCP is no longer listed. Note that this is possible because active ingredients (i.e. drugs) are not required to be labeled on <u>all</u> products.

Types of products that have been known to be manufactured with more than .75% by weight HCP are listed in Table 1. Other types of products where certain brands have contained HCP but the quantity was not indicated on the preliminary FDA list (6) are shown in Table 2.

Background

Hexachlorophene is a white, crystalline, odorless substance that is insoluble in water; its chemical formula is $C_{13}H_6O_2Cl_6$; using one system of nomenclature its full name is bis-(3,5,6-trichloro-2-hydroxyphenyl)-methane (7). Other names are 2,2-methylenebis-(3,4,6-trichlorophenol), 2,2-dihydroxy-3,5,6,3',5',6'-hexachlorodiphenylmethane and "G-11". Meeting the criteria of a) being non-reactive with soaps or soap constituents, b) neither being volatile nor having a disagreeable odor, c) being non-toxic for external use and d) not causing stains on the skin or spots in laundry, the bactericidal properties of HCP promoted its use first in cakes of soap and then in an ever widening array of over-the-counter drugs and cosmetic preparations. Since its first use following development and toxicity testing over twenty-five years ago, HCP has been used in soaps, detergents, shaving preparations, dental cleaning preparations, first aid creams, acne preparations, personal deodorant products (roll-ons, creams, sprays, including feminine hygiene sprays), baby products (powders, creams etc.), and almost every type of product generally considered cosmetics - rouges, face powders, makeups as well as in hair preparations (8). Any preparation used somewhere around or on the body might contain HCP.

Manufacturers use HCP either as a preservative, usually in concentrations of about .1% by weight, or for its ability to cause decreases in skin surface resident, gram positive bacteria (7). This latter property has led to the use of products containing 1-3% HCP as a surgical scrub and for cleansing new born infants. Non-human contact products such as shoe liners or household air filters have also been treated with HCP because of its bacteriostatic properties (9, 10). The effectiveness of HCP as an antibacterial agent is closely coupled to its proven long term retention on the skin surface after washing; its presence has been detected after rinsing (7).

The leading manufacturer of HCP advertised it as "the 'proven one'", boasting of its widespread use and ubiquitous safety (9). Extensive studies justified their claims (7). As long ago as 1959, however, there were specific incidents which began to create doubts about HCP's universal safety. Infant convulsions, and adverse skin reactions on human beings, and brain lesions in test animals were linked to HCP. It was detected in the blood of infants (at levels close to internal toxicity levels) that were bathed in soaps containing HCP (17). On November 28, 1971 the Health Research Group (11) asked the Food and Drug Administration to ban the use of HCP.

Some consumer groups felt the FDA responses which followed the re-evaluation of HCP toxicity were insufficient (7) while individuals and special interests complained that the FDA had over-reacted (2, 10). On December 12, 1971 the FDA issued a recommendation against the generalized bathing of newborns, and convened an investigatory panel. A proposed limitation of .75% as an active ingredient and .1% preservative limitation for HCP was published by the FDA in the Federal Register on January 7, 1972 (12).

Subsequently outbreaks of staph infections in hospital nurseries were blamed on the lack of HCP usage (3). While the FDA limited use on bathing newborns, the restrictions specifically suggested continuing usage on hands and nursery objects that would come in contact with the infants. Hospitals where infections broke out had usually stopped the use of HCP soaps for all uses around the nursery.

New evidence pointed to HCP as the culprit in other cases. Multiple baby deaths in France were linked to baby powder that accidentally contained 6% HCP. A University of Washington researcher demonstrated that microscopic slide examination of the brains of dead infants that had been bathed with HCP contained the same brain lesions previously seen in test animals bathed with HCP (1, 2, 13). On September 22, 1972 the FDA published more stringent regulations (14) on the use of HCP to take effect with their publication in the Federal Register on September 27, 1972 (3, 15).

Hexachlorophene Recalled

FDA press releases announced the restrictions on September 22, 1972 to be effective September 27, 1972. A TWX (teletype) release went to FDA regional offices and NYS Health offices that have this facility (16). (Monroe County is one of the few County Health Departments that has a TWX.) Some field offices of the FDA had to await a mailing; these offices often get notified about FDA rulings from the press or from an interested individual in the community before they receive word officially.

Since by itself, HCP is a drug, manufacturers are listed with the FDA and were notified directly. The FDA, however, had no record of everyone who used HCP in their products (4). The FDA had to rely on the HCP manufacturers to notify their clients. Since this was of limited effectiveness, the FDA requested its regional offices to conduct a field investigation of all potential product manufacturers that the regional officials could think of within their territory. This information on HCP products is being compiled by the FDA and used to prepare a list (6) of products and their HCP content. This process was not complete two months after the ban went into effect (6).

Although retail stores might suspect a product as containing a forbidden amount of HCP, unless they are notified they will not know that it should be taken off the shelf. Lists of the HCP content have not been locally available. Therefore, consumer groups have been compiling their own lists of known or suspected greater than .75% HCP products (17). Storekeepers have sometimes refused to remove such products when notified by consumer groups. Filing individual complaints with the FDA to force removal is a long slow process (4). While some delay in banned product removal might be acceptable, such products have been found on the market shelf one month after the ban (17). There is no guarantee that banned products will not be found on the shelf for a long time after the deadline. When NTA containing detergents were voluntarily dropped by the manufacturers, these products were found on the shelf one year later (18). Since there will be no store by store, shelf by shelf inspection, in some cases products with greater than .75% HCP will only disappear by attrition as will all the .1 - .75% HCP products. Caveat emptor!

The new ban on all HCP in such products as chapsticks, feminine hygiene sprays, and rectal ointments, that is any product used on or around mucous membranes, represents a special problem. While new, manufactured after November 4, 1972 supplies of these products with .1% or less HCP will not be restocked, such products were allowed to be made and shipped after the original ban of September 27, 1972. Although all stocks which met the original limitations may have been eliminated from the shelves, these newly proscribed products will still be available until present supplies are exhausted.

Feminine Hygiene Sprays

These products, packaged in aerosol spray cans and containing HCP, have been the source of an abnormally large number of complaints due to adverse reactions (19). Their efficacy is doubtful.

What is more important than the percentage of HCP is the residual amount left on the skin (10). Percent contents is regulated because it is more easily controlled. Feminine hygiene sprays are especially notorious because they are not washed off and are applied to or near mucous membranes. Both these conditions tend to maximize rather than minimize the amount of HCP that might be absorbed into the blood. Feminine hygiene sprays have not been subject to the regulations that would require type and amount of active ingredients to be on the label. Since there is no medicinal claim, they are usually considered as cosmetics.

Under the September 27, 1972 rules, HCP percentage was measured for aerosols by comparing the weight of the HCP to the weight of the total contents minus the propellant. Some manufacturers suggested to the FDA that the propellant be added into the calculation. This had the effect of increasing the amount of HCP allowed. This proposal was challenged by the Health Research Group (20).

On November 4, 1972, new rules (21) were issued for HCP in products that might be used on or near mucous membrances, i.e. feminine hygiene sprays. In these products no HCP will be permitted at all. Other aerosols will now be permitted to contain .1% HCP on a strictly weight/weight basis without the previous deduction of the propellant. Thus while the consumers will be protected against HCP in feminine hygiene sprays, they may be threatened by more HCP in other aerosol sprays such as under-arm deodorants and hair sprays. Also, there is the further problem that retailers may have removed their HCP stock from their shelves during the less restrictive period (September 27 - November 4, 1972) and so, some banned feminine hygiene sprays may remain on sale. For these reasons, consumers must be even more vigilant if they wish to use only those products which contain only the amount of HCP (or none at all) permitted for newly manufactured products.

Table 1. Types of products that have contained more than .75% hexachlorophene.

creams	suppositories
lotions	body and foot powders
cleansers	ointments
soaps (household bar type and surgical)	toothpaste
shampoos	sprays

"acne" and "medicated" are words often associated with these products

Table 2. Types of products, not previously mentioned in Table 1, known to contain hexachlorophene where the content is as yet unknown.

burn sprays and lotions
medicated sticks
antiperspirant/deodorant products (creams, rollons, sprays, sticks)
hand lotion
hand creams
makeup preparations of many types
other antiseptic products
sunburn products
bath oils
denture products
toothache jel
hair removing products

NB. these types are to be considered broad, general categories - i.e. medicated sticks include blemish covering, acne, shaving, etc. products based on a tentative FDA list of brand vs concentration (when known) of HCP (14).

References

(1) Business Week, September 30, 1972 p 24

(2) Wall Street Journal, September 25, 1972

(3) Federal Register, vol. 37, #188, Wednesday, September 27, 1972, p 20160

(4) private communication with Mr. Matlock, FDA Buffalo

(5) Food, Drug and Cosmetic Act, 21 U.S.C.

(6) private communication, Mr. Ed Nida, FDA - Rockville, MD.

(7) "The Story of Hexachlorophene," Soap and Chemical Specialties, October, 1970 p 58. The authors are the research group at Givaudan Corp., the leading developer and producer of hexachlorophene.

(8) Clinical Toxicology, 1969

(9) advertisement for G-11, the Givaudan brand of hexachlorophene, Soap and Chemical Specialties, October 1970, p 22.

(10) Wayne L. Pines, FDA Papers, April 1972, p 11. "The Hexachlorophene Story", a review by an FDA staff member.

(11) private communication - Health Research Group, 2000 P St. NW, Washington, D.C. to FDA

(12) Federal Register, vol. 37, #4, Friday, January 7, 1972, p 219

(13) Science, September 1972 p 1175

(14) FDA Fact Sheet - Hexachlorophene, DHEW publication (FDA) 73-3004

(15) Authority for the FDA to do this is contained in chapter 21 of the United States Code which includes the Food Drug and Cosmetic Act as amended. The FDA rules for hexachlorophene became section 3.91 of Chapter 21, Code of Federal Regulations, (21CFR 3.91)

(16) pr # 72-82 (FDA), September 22, 1972

(17) private communication, Judy Braiman

(18) private communication, Dr. K. Harbison

(19) Consumer Reports, January 1972, pp39-41

(20) private communication, Health Research Group, 2000 P St. NW, Washington, D.C. to the FDA, Rockville, MD, October 20, 1972

(21) Federal Register, vol 37, No. 214 - Saturday, November 4, 1972