UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

July 24, 1997

Mr. Peter W. Colby
Colby and Nance, L.L.P.
1001 G Street, NW, Suite 400 East
Washington, DC 20001

Dear Mr. Colby:

Thank you for your letter to Rick Brandes of January 23, 1997, in which you asked for a regulatory determination on the status of certain manufacturing wastes. Specifically, you wanted to know: 1) if warfarin tablets subject to "dissolution testing" are considered hazardous wastes, 2) if fragments from integrity testing of tablets are considered hazardous waste, 3) if certain wash down water is exempt from the mixture rule; 4) the regulatory status of disposable gloves and other personal protective equipment; 5) the status of wastewater from the cleaning of gloves and protective equipment, and 6) if air filters removed from the ventilation system in the manufacturing process are considered hazardous waste.

We have considered the views expressed in your letter and provide the following response based on a general principal: in interpreting the hazardous waste regulations at 40 CFR 261.33, EPA takes the position that a point exists in the manufacturing process in which an operator creates either a commercial chemical product or manufacturing intermediates. When these chemicals meet a listing description under 40 CFR 261.33, any discard of these materials (including these materials captured on filters or mixed with other wastes) are considered hazardous wastes and must be handled accordingly.

Under 40 C.F.R. 261.33, EPA may list as RCRA hazardous wastes various materials associated with chemical products that become hazardous wastes if and when they are discarded or are intended to be discarded. Acutely hazardous chemical product wastes are listed in section 261.33(e) and are known as "P-wastes." Other hazardous chemical product wastes are known as "U-wastes" and are listed at section 261.33(f). Not all P or U listed substances wherever found, however, are RCRA chemical product hazardous wastes. A particular substance is a P or U waste only if, before discard, it is the sole active ingredient in a "commercial chemical product or manufacturing chemical intermediate." See 40 C.F.R. 261.33(a) through (f).

The term "commercial chemical product or manufacturing chemical intermediate" is interpreted in the "Comment" in 40 C.F.R. 261.33(d). The term refers to a chemical "manufactured or formulated for a commercial or manufacturing use" which consists of the commercially pure or technical grades of the chemical and "all formulations in which the chemical is the sole active ingredient." This is distinguished from a chemical contained in a manufacturing process waste. Process wastes are generated

prior to the creation of the product or intermediate and may be listed as F or K wastes under EPA's listing system.

Once a commercial product or manufacturing intermediate is created, a RCRA hazardous waste is generated when any of the materials related to the product (as described in section 261.33(a) through (f)) is discarded, or intended to be discarded. Because all the activities in your letter describe discarded materials in one form or another, if a commercial chemical product or manufacturing intermediate containing warfarin as its sole active ingredient has been created before any of the activities you describe, the waste must be treated as a RCRA hazardous waste unless an exemption can be found. Further, your description of your client's operation as one in which warfarin is not manufactured, but rather is simply processed into products from warfarin manufactured at another site, suggests all waste not otherwise exempted would qualify as hazardous because the warfarin enters the operation as a commercial chemical product.

In your letter, you characterize waste from dissolution testing (i.e., placing tablets in a distilled water solution and observing the results) and integrity testing (crushing or breaking tablets into fragments) as manufacturing process waste and/or used commercial chemical products. This interpretation is incorrect. Once the product is manufactured, then the listing of a commercial chemical product under 40 CFR 261.33 attaches. As a practical matter, the crushed or dissolved waste would be expected to have the same sort of composition and pose the same sort of threats when discarded as would the untested commercial product and thus must be managed as a hazardous waste listed under 40 CFR 261.33.

Your statement concerning the applicability of the de minimis exemption under 40 CFR 261.3(a)(2)(iv)(D) to plant wash down water may be correct. The exemption applies to discarded commercial chemical products or chemical intermediates listed in §261.33 from manufacturing operations in which the materials are used as raw materials or are produced in the manufacturing process. The regulatory language in §261.3(a)(2)(iv)(D) provides several examples of de minimis losses envisioned by the regulatory exemption. Please remember the facility's discharge of wastewater must be subject to regulation under Section 402 or 307(b) of the Clean Water Act to qualify for this exemption. Also, please be aware that if the facility's wastewater treatment system leaks before the wastewater reaches the headworks of the treatment system, the leaked material is classified as a §261.33 material. In addition, while the de minimis amount is not quantified in the regulatory language, large material losses would void the de minimis quantity exemption.

As for wastewater from the cleaning of protective equipment, the regulatory language of §261 .3(a)(2)(iv)(D) includes "discharges from... rinsing and cleaning of personal safety equipment..." Again, if the cleaning was done on the facility's site and the discharge of wastewater met the requirements for exemption above, the wastewaters would be exempt from the mixture rule.

With respect to the equipment, itself, the analysis should begin with an evaluation of whether the substance that comes in contact with the equipment consists of small amounts of the actual formulated commercial chemical product or manufacturing intermediate (not manufacturing process wastes). If this is the case, the discarded equipment is debris (a “manufactured object” as described at 40 CFR section 268.2(g)) containing a listed hazardous waste—discarded product or intermediate. It, therefore, must be managed as a hazardous waste until it no longer “contains” the hazardous waste. See 57 FR 958 at 986 (Jan. 9, 1992).

There is no explicit exemption for discarded equipment contaminated with de minimis losses from manufacturing operations. However, the contaminated equipment could be washed to the point that it is

considered to no longer "contain" the hazardous waste. This interpretation is based on the fact that the equipment would qualify as hazardous debris under 40 CFR sections 268.2(g) and (h). Under section 261.3(f)(1) it would not be subject to regulation as a hazardous waste if it is washed using one of the technologies described in section 268.45, Table 1. See, in particular, physical and chemical extraction technologies.

Whether air filters from the manufacturing process that contain warfarin should be managed and disposed as nonhazardous waste depends on site-specific details. We would suggest you review the specific circumstances with the appropriate State agency. As we understand your letter, warfarin is released as it is prepared in a separate, sealed-off area. Air filters used in the chemical production of a commercial chemical product or manufacturing intermediate meeting a P or U listing prior to creation of such product or intermediate are considered manufacturing process wastes which do not fall within the listing under 40 CFR 261.33. However, once the material starts to met the listing description as the commercial chemical product or manufacturing chemical intermediate, the particles of warfarin, or of formulations meeting a P or U listing description captured by the filters, still constitute the listed commercial chemical product subject to regulation as hazardous waste, when disposed. The air filters are also subject to regulation as hazardous waste when disposed because they would constitute a solid waste mixed with a listed hazardous waste. The air filters, however, like the personal safety equipment, may also be able to qualify as hazardous debris and may be washed to remove the hazardous waste.

The specifics of how your situation apply to the principles stated above should be reviewed by applicable State Agencies. Please check with the State in which your client's facility is located with respect to the application of general principles to the specific circumstances at your facility and to make sure that other restriction do not apply.

Thank you for your inquiry. If you have any additional questions on this topic, please call Rick Brandes of my office at (703)308-8871.

Sincerely,

David Bussard, Director Hazardous Waste Identification Division

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January 23, 1997

Mr. Richard Brandes
Chief, Waste Identification Branch
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Re: Request for Classification of Manufacturing Waste

Dear Mr. Brandes:

We represent a drug company that is manufacturing a product whose sole active ingredient is warfarin sodium. Currently, the manufacturer manages and disposes of all warfarin-containing waste that is generated through compounding and laboratory operations as RCRA hazardous waste. However, based on our analysis of the federal regulations, it appears that several of the waste streams need not be managed as hazardous. We would appreciate learning the Agency's position as to whether the waste streams discussed below must be managed as hazardous under EPA's RCRA regulations.

DISCUSSION

The product at issue contains between .45% and 4.5% warfarin sodium (depending on the dose) as its sole active ingredient, and will be marketed under the name "warfarin". Accordingly, there is no question that the finished product qualifies as a hazardous waste under 40 C.F.R. 261.33(e) ("commercial chemical product") when it is disposed of for being off-specification or otherwise in a manner that falls within the listing. Likewise, the active ingredient warfarin sodium, which is purchased by our client for use in the formulation of the drug, is a commercial grade chemical that falls within the listing in 40 C.F.R. 261.33(e) when it is disposed of in accordance with the terms of the listing.

The issue on which we are seeking guidance is whether certain wastes containing warfarin which are generated in the quality assurance/quality control process or in the compounding process fall within the commercial chemical product listing. Of course we are aware that even if these waste streams do not fall within the commercial chemical product listing, they may fall within some other listing or may exhibit a hazardous characteristic. However, we are not seeking the Agency's position on any other such issues in this letter.

QUALITY ASSURANCE/QUALITY CONTROL WASTE

1. Dissolution Laboratory Waste

As a part of its quality control procedures under FDA requirements, the manufacturer routinely tests samples of the finished warfarin tablets to determine how fast they will dissolve after ingestion. Dissolution testing is accomplished by placing tablets in distilled water for a standard period of time and observing the results. After the testing is completed, laboratory personnel dispose of the test solution of water and drug ingredients, currently as hazardous waste.

According to our understanding of the commercial chemical product listing, this waste does not fall within the listing. The commercial chemical product listing is limited to a manufactured product that is disposed of under specific circumstances listed in the regulations, including when the waste is off-specification, contaminated, or spilled. See 40 C.F.R. 261.33(a)-(d). The listing does not encompass every waste, "such as a manufacturing process waste", that contains the listed chemical. 40 CFR 261.33(d) *(comment)*. Here, the residue produced by a quality control is essentially a manufacturing process waste, and its disposal does not fall into any of the categories in the listing regulation. Therefore, the waste should not be considered hazardous under the commercial chemical product listing.

Moreover, although the listing regulation does not state that the commercial chemical product must be "unused", EPA has interpreted the listing as being limited to "unused chemicals". *Nitroglycerin Pills as Commercial Chemical Products,* September 1993 Monthly RCRA Hotline Report. Under the facts set out above, testing should be considered the equivalent of use, since the manufacturer has deliberately altered the product physically or chemically in order to serve a specific goal. Thus, the dissolution laboratory waste should not be considered to be within the commercial chemical product listing, and can be discharged to the local sewer system.

2. Integrity Testing Waste

The manufacturer also conducts physical integrity testing for quality control purposes. The manufacturer selects a sample of tablets and subjects them to controlled pressure in order to determine how well they will withstand physical chipping and breaking. When the test is completed, the manufacturer disposes of the resulting dust and fragments as hazardous waste.

Just as with the waste generated by dissolution testing, the disposal of this waste does not fall within any of the categories specified in the commercial chemical product listing. Likewise, the dust and fragments are analogous to a used or spent product, since they have been used for the intended purpose of quality control. Therefore, the waste from integrity testing should not be considered to be within the commercial chemical product listing.[i]

MANUFACTURING WASTE

Waste that is generated in the process of manufacturing warfarin tablets for sale presents different issues. The basic process is simple; the warfarin sodium is blended with various inert ingredients (primarily lactose, starch and water) and the mixture is physically converted to granular form. The granules are dried and then compressed into tablets. Three main waste streams are generated: (1) washdown water containing residues of

warfarin and other drug ingredients, which is generated by cleaning machinery, containers, implements, and manufacturing rooms, (2) disposable gloves, gowns, and other personal equipment used by employees in the manufacturing area, all of which contain traces of warfarin, and (3) airborne dust that is collected in air filters, which are periodically replaced and discarded.

1. Washdown Water

The commercial chemical product listing specifies that not all manufacturing process wastes containing chemicals on the list are thereby rendered hazardous. 40 C.F.R. 261.33(d) *(comment)*. However, the listing itself gives no guidance as to which types of process waste, if any, are to be considered hazardous.

The separate regulations defining hazardous waste contain an exclusion for “de minimis losses" of a listed commercial chemical product that occur when the listed product is used as a raw material or produced in a manufacturing process, so long as the de minimis quantities are discharged to the sewer system. 40 C.F.R. 261.3(a)(2)(iv)(D). The regulations state that de minimis losses include spills from normal material handling operations such as the transfer of materials, leaks from pipes or process equipment, sample purgings, and discharges from safety showers and rinsing and cleaning of containers and personal safety equipment.

This exclusion should apply to washdown water generated in the manufacture of warfarin when the wastewater is disposed of through the sewer system, as this waste constitutes a "de minimis" loss from manufacturing. Moreover, the waste falls clearly within EPA's rationale for the regulatory exclusion:

> These small losses of raw materials, products or intermediates are often disposed of by draining or washing them into the wastewater treatment system. This typically is a reasonable and practical means of disposing of these lost materials. Segregating and separately managing them often would be exceedingly expensive and may not be necessary because the small quantities can be assimilated and treated in the wastewater treatment system.

46 Fed. Reg. 56582, 56586 (November 17,1981). In addition, the Agency has noted, because these losses constitute waste of a valuable product, the manufacturer has a strong incentive to minimize the amount that is lost.

Here, despite the efforts of the manufacturer to minimize waste, the washdown water still contains small quantities of warfarin. The washdown water is currently collected and disposed of as hazardous waste at considerable expense. However, since the small amounts of warfarin found in the washdown water fall within this regulatory exclusion, the manufacturer should be allowed to modify its procedures and dispose of the washdown water through floor drains or otherwise into the sewer system.

2. Disposable Gloves and Other Personal Equipment

According to the regulatory exclusion discussed above, wastewater generated from cleaning gloves, gowns, and other reusable personal equipment would be excluded from the commercial chemical product listing if the wastewater were discharged to the sewer. 40 C.F.R. 261.3(a)(2)(iv)(D). In this case, as a result of FDA requirements, the manufacturer uses disposable gloves and other protective equipment to avoid any risk of contaminating the product. As a result, instead of generating wash water, the manufacturing process generates dry disposable materials that contain traces of warfarin.

Disposable gloves and other personal equipment with traces of warfarin should be subject to management and disposal as nonhazardous solid waste. As a practical matter, this is appropriate because the waste presents the same minimal threat to human health and the environment as the de minimis losses discussed above. Because of the way the waste is generated and the manufacturer's incentive to minimize the lost product, the waste will contain very small amounts of the listed commercial chemical product. Moreover, when the waste is landfilled, the traces of warfarin will soon be diluted or broken down into other substances, just as when wastewater containing trace amounts of product is discharged to the sewer system.

There are at least two ways to analyze this issue under the regulations. First, the waste (defined as "disposable personal protective equipment containing traces of warfarin") can simply be deemed to fall outside the commercial chemical product listing. The waste is not a "commercially pure grade of the chemical" nor a formulation in which the chemical is the sole active ingredient", nor does it fall within any of the other categories enumerated in 40 C.F.R. 261.33. Under this analysis, the waste is simply not a listed hazardous waste, and no exclusion is required.

This issue also could be analyzed under EPA's "contained-in policy". Under this analysis "debris", including clothing and other manufactured items that are being disposed of may be considered hazardous if it contains hazardous waste (here, the traces of warfarin). If the debris were considered potentially hazardous under the contained-in policy, then the state regulatory agency would have the option of determining whether the specific waste stream should in fact be considered hazardous, based on either site-specific or contaminant specific concentration levels. Under this scenario, then, the applicable state agency would have the ultimate decision making authority as to whether the waste should be managed as hazardous. On these facts, the agencies should allow the waste to be managed as non hazardous.

3. **Air Filters**

The area in which the warfarin is manufactured is sealed off from the remainder of the facility, and has a separate ventilation system. The air is continually filtered to remove any impurities, including traces of warfarin that may have become airborne during the manufacturing process. The air filters are periodically removed from the ventilation system and disposed of.

The air filters should be analyzed in essentially the same way as the disposable gloves and other personal protective items. The simplest approach would be to determine that the filters fall outside the commercial chemical product listing. An alternative would be to analyze the filters under the contained-in policy, so that the applicable state agency would determine whether they need to be managed as hazardous waste. In either case, based on the particular facts involved here, the air filters should be managed and disposed of as nonhazardous solid waste.

CONCLUSION

We would appreciate hearing EPA's interpretation of the RCRA regulations as they apply to these issues. If you need further information, please do not hesitate to call me. Thank you for your assistance.

[i] If EPA concurs in this conclusion, the integrity testing waste will be sent for incineration along with all the other nonhazardous pharmaceutical waste that the manufacturer generates.