DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612 (949) 608-2900 Fax:(949) 608-4417 Industry Information: www.fda.gov/oc/industry	05/26/2009 - 05/28/2009* FEI NUMBER 3007187671

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Tim L. Clarot, Vice President R&D and Product Quality

FIRM NAME	STREET ADDRESS
Matrixx Initiatives Inc	8515 E Anderson Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Scottsdale, AZ 85255-5461	Drug manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

OBSERVATION 1

Serious adverse event(s) for a non-prescription drug used in the United States has not been reported to the Secretary.

Specifically,

The firm does not classify and report anosmia (loss of smell) or loss of taste as a serious adverse event and therefore does not report these complaints to the Food and Drug Administration (MedWatch reporting system). The following three complaints were not reported to the Food and Drug Administration (MedWatch reporting system): AE09-000723, AE09-000736 and AE09-000886.

*** DATES OF INSPECTION:**
05/26/2009(Tue), 05/28/2009(Thu)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Timothy T Kapsala, Investigator Timothy T. Kapsala	05/28/2009

SUMMARY

This was the initial inspection of an own label drug distributor, under PAC 56002, FACTS assignment #640643, per LOS DO work plans for FY '05. The inspected site is a corporate office at which some relevant records & labeling are stored or easily accessible, including complaint records. OTC drug cold/allergy products, mostly homeopathic but not low dose, are made by various contractors and are not stored or analyzed at the inspected site. Therefore, the inspection was limited mainly to the firm's Quality System, and, within that, mainly to complaint procedures & records, & follow-up by the firm, due to previous Medwatch & consumer complaints concerning anosmia (loss of smell/taste) upon use of zinc-containing oral & nasal products. Complaint data provided indicate that some degree of anosmia, of either short or long-duration, is complained of by about 3.6 persons for every 100,000 units sold of the firm's two largest selling nasal zinc products, nasal swabs and nasal spray, which together account for about (b) (4) units sold from '99 –'05. The peak rate was about 6.7 per 100,000 during 2004, which management said was caused primarily by a negative television show during early 2004.

Sample DOC 86333 was collected for label review of homeopathic OTC status per the Homeopathic Pharmacopeia: its monograph for zinc gluconate and its definition of zinc gluconate as a class F solid product.

A 1- item FDA 483 was issued concerning failure to fully complete a particular data field on numerous complaint forms in 2005. Management states that they have been working with a new complaint handling contractor since late 2004 and have not yet smoothed out all procedures. Management promised a review of Matrixx's needs, as well as data fields, data screens, training at contractor, etc will be conducted, with appropriate form/field revision and retraining as needed at the contractor. Management is also reviewing and revising the written complaint procedure & will attach it to a written response to the FDA 483.

FMD 145 or other correspondence may be sent to Carl J. Johnson, President & CEO, Matrixx Initiatives, at the address immediately below.

ADMINISTRATIVE DATA

Inspected firm:	Matrixx Initiatives, Inc. AKA Zicam LLC
Location:	4742 N 24th St Ste 455 Phoenix, AZ 85016-4856
Phone:	602385-8888
FAX:	
Mailing address:	4742 N 24th St Ste 455 Phoenix, AZ 85016-4856
Dates of inspection:	5/25/2005, 5/26/2005, 5/27/2005
Days in the facility:	3
Participants:	Randall N. Johnson, Consumer Safety Officer

HISTORY

This firm has not previously been inspected by FDA.

The firm is an own-label distributor of cold/allergy/nasal remedy drugs. The firm employs (b) (4) people, all at the inspected corporate headquarters address. (b) (4) (b) (4) (b) (4) The firm (b) (4) (b) (4) develops & approves the labeling for its products.

The firm is incorporated in Delaware. This publicly traded corporation, traded on NASDAQ, originated in Phoenix during the late 1990's, when it was originally known as Gumtech. Matrixx later split from Gumtech, with Matrixx buying out a portion of Gumtech known as Geltech/Biodelivery. (Gumtech remained in business for a while, and was purchased by (b) (4) with an eye towards chewing gum as a drug delivery system, but went OOB after a while.) A web-news item concerning the name change form Gumtech to Matrixx is attached as part of Exhibit 12a.

Matrixx Initiatives, Inc., operates a single wholly-owned subsidiary, Zicam LLC. Matrixx operates as a parent corporation with an eye towards eventually opening other wholly-owned subsidiaries, with no firm plans for such, yet.

The officers for Zicam are the same as those for Matrixx, as given below under Individual Responsibility.

The firm specializes in cold/allergy/nasal remedies, as given on the product list (Exhibit 13). Six of these, under the "Cold Remedy" product line, contain zinc compounds and are labeled as homeopathic drugs. They are not necessarily of low concentration, however: for example, (b) (4) the nasal gel (delivered via pump bottle similar to a standard nasal spray bottle) contains about 2 mg/mL of elemental zinc according to analytical certificates attached to this report (EX. 19). The nasal gel pump has been sold since 1999 and has sold (b) (4) units nationwide. Nasal gel swabs, (b) (4) (b) (4), have sold since 2002, with about (b) (4) units sold, so far. Currently, (b) (4) drug store chain is a major distributor.

The firm experienced some negative publicity on television (Good Morning America) and through other media during early 2004, concerning cases of anosmia (loss or reduction of smell/taste) in users of Cold Remedy products. See Exhibits 8, 9a, 9b, 9c, and 11 for some background information. (Complaints were the major focus of the current inspection.)

Hours of operation: (b) (4)

Registration: The firm last registered during April 2004. I advised the firm to reregister due to its involvement in product formula development & approval and in labeling design & approval.

INTERSTATE COMMERCE

One major distributor of the Matrixx product line is the (b) (4) drug store chain.

The firm contracts out (b) (4) See the list of firms attached as Exhibit 20. Almost all are (b) (4), including the manufacturer/filler/packagers.

The (b) (4) manufacturers of nasal gel swabs and nasal gel pump are (b) (4) (b) (4); and (b) (4) (b) (4), addresses given on Exhibit 20.

DOC 86333 of Cold Remedy Nasal Gel (pump version) was collected for label/regulatory review. Interstate documentation is attached to that collection report.

JURISDICTION

A list of drug products is attached as Exhibit 13. Labels for the Cold Remedy products are attached as Exhibits 22-27. Also see Interstate Commerce, above.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

I displayed my credentials and issued Notice of Inspection to Timothy L. Clarot, Vice President, Research and Development, on 5/25/05. He provided the majority of information during the inspection and was present at the FDA 483 presentation. Due to illness, the firm's President and CEO, Carl J. Johnson, was not available for most of the inspection, but was briefly present at the firm at various times. He was not present at the FDA 483 presentation.

PERSONS INTERVIEWED:

(b) (6), who is administrative assistant to Mr. Clarot, according to the organization chart (EX 12c), provided many documents and much information during the inspection concerning complaints, computer systems, and (b) (4) which is t(b) (4) for Matrixx. (b) (4) to the firm's

master computerized complaint data system, the "back end" system, described below under "COMPLAINTS"

Louise Wojcik, Manager of Quality Control/Quality Assurance, also provided some information and documents during the inspection. She answers to Mr. Clarot.

RESPONSIBILITY:

The firm's organization chart is attached as Exhibit 12c; selected portions of the annual report, including a listing of the board of directors, are Exhibit 12b. The chairman of the board is Edward E. Faber. Carl Johnson is a member of the board.

The firm employs (b) (4) persons, all at the inspected site.

Mr. Clarot said that no single person owns a controlling interest in this publicly traded corporation. He estimated that the most stock anyone owns might be as great as (b) (4) % of the stock.

Expenditures: there is a regular annual budgeting process. The Board ultimately approves any major capital expenses, such as, say, a new computer system, that might be outside routine annual operations budgeting processes. (b) (4)
(b) (4)

According to Mr. Clarot: Mr. Clarot reports to Mr. Johnson. Mr. Johnson answers to the board. However, Mr. Johnson is more or less the ultimate authority at the firm, in terms of product line and overall market strategy.

(b) (4)

The firm develops its labeling, approves labeling, (b) (4)

FIRM'S TRAINING PROGRAM

I did not inspect this during the inspection. The possible need for retraining of employees, especially at the contract complaint organization, was discussed. See "Objectionable Conditions & Management Response", below.

MANUFACTURING/DESIGN OPERATIONS

This was an inspection of a corporate office. All operations are contracted out, as described in various sections of this report.

MANUFACTURING CODES

Codes for the two principal zinc product manufacturers are attached as Exhibits 28 and 29.

COMPLAINTS

Complaints and the firm's complaint system were the principal focus of the inspection at this own label distributor's corporate office.

Products are manufactured (b) (4) (b) (4) Distributors are also listed on Exhibit 20. The inspected site rarely receives or handles products, except for partial lots used by sales staff and the like, e.g., as demonstration items or as samples for potential customers. The QA and QC staff at the inspected site are involved in the complaint system; see Exhibit 1, which is the firm's complaint procedure, and see the organization chart, Exhibit 12c (Louise Wojcik, QA/QC Manager at Matrixx, is Matrixx's QA/QC staff). Also see the firm's product list, Exhibit 13. (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) to receive and record complaints. Mr. Clarot said that the employees at (b) (4) who handle Matrixx complaints are (b) (4) this group is currently supervised by (b) (4) Matrixx's product carton labels and

immediate container labels list a toll-free telephone number that connects the caller directly with (b) (4)

One of these is a registered nurse at (b) (4), who receives, evaluates, tracks, and closes safety complaints, and who also prepares the (b) (4) chart used for tracking anosmia complaints, example attached as Exhibit 16. He/she also takes initial calls from, or recontacts, those with anosmia complaints to obtain information for the anosmia questionnaire (EX. 15). He/she (currently (b) (6)) decides on the need for follow up. (See "OBJECTIONABLE CONDITIONS & MANAGEMENT RESPONSE", below, for the FDA 483 item concerning the complaint form, and need for follow up as listed on the complaint form and as discussed within the SOP.)

The complaint SOP is Exhibit 1. The two varieties of "Form A", the complaint form, are attached as Exhibit 2. They are not as seen on-screen by complaint entry operators at (b) (4); see Exhibit 2a for an on-screen view. Information is the same on both printed forms except for the lack of codes on one variety, which is accessible to and used by Matrixx's (b) (4) The coded variety is used by Matrixx's QA staff and can be accessed/printed by (b) (4) (b) (6) (See EX. 14 for codes). Both varieties of form are derived from the same source information entered by (b) (4) personnel when complaints are received.

Complaints gathered by (b) (4) are available to Matrixx through two pathways. Uncoded complaint information is regularly transferred from (b) (4) to the (b) (4) database, (b) (4) (b) (4) And, at the end of each work week (b) (4) (b) (4), the same information, along with complaint codes as described in Exhibit 14, is downloaded by (b) (4) (b) (4) into a complaint database at Matrixx, called the "back end" data system, which contains all computerized complaints gathered previously by (b) (4) (b) (4) (b) (4) (b) (4) (b) (6) has password access to this system, according to both (b) (6) and Mr. Clarot. During the inspection, printouts of coded complaint forms (Form A) from the 'back end' data system, as well as various printouts of sort/filter operations from this database, were obtained for me by her.

Louise Wojcik, Manager of QA/QC, said that she reviews complaints at least weekly. She said that the nurse at (b) (4) will inform Matrixx ASAP of any serious injury situations. Mr. Clarot said that he also reviews the electronic log of complaints regularly.

Complaints and the firm's complaint system were the principal focus of the inspection of this own label distributor's corporate office. The 1-item FDA 483 concerns the complaint SOP (EX. 1); examples of the complaint form demonstrating the FDA 483 item are attached as Exhibit 3. Various examples and versions of the complaint form are attached as Exhibits 2, 2a, 3, 3a, 3b, and 14a. Complaint coding can be found in Exhibit 14. Explanations of the exhibits are found within the EXHIBITS listing, below, and within "OBJECTIONABLE CONDITIONS and MANAGEMENT RESPONSE", below.

Many other exhibits attached to this report directly or indirectly concern the complaint system as well as various Medwatch reports, and consumer complaints received by FDA; please see the EXHIBITS list below for a full listing of this report's many exhibits.

During preparation for this inspection, I came across a number of printed Medwatch forms (origins not fully known, but apparently printed at a previous time at PHX RP in anticipation of a possible inspection at Matrixx), as well as a number of consumer complaints listed within the FACTS system. The consumer complaints had been "closed", but I selected a number for at least brief review during the inspection, if they were not too old (i.e., preferably within the last two years) and if the consumer had provided enough information for follow up, especially the lot number of the product. I used the same approach when selecting Medwatch reports for review, along with the additional criterion of legibility of the printed copies available to me.

After reviewing the complaints/reports and making a trip to a (b) (4) drug store in Scottsdale, AZ to examine ingredients listings and other labeling on Matrixx products, I focused upon the anosmia complaints and zinc-containing products. Exhibit 13 lists all 16 of the firm's products (although it highlights only 15 of them). Six of these products, all under the general label/product line known as "Cold Remedy", contain zinc, as either zincum gluconicum and/or zincum aceticum, homeopathic nomenclature for zinc gluconate and zinc acetate. The products are delivered as a nasal gel (somewhat like nasal spray), nasal swab, oral mist, chewable, and lozenge. Labels/labeling for these six products are attached as Exhibits 22 – 27. I also collected DOC 86333 for review of homeopathic/OTC status of the firm's (b) (4) the Cold Remedy nasal gel.

For the most part, my review of the above complaints consisted of requests for certificates of analyses performed by the contract manufacturers, and of a general review of the method by which complaints are received, logged, tracked, and trended by Matrixx. Analyses of zinc & pH were within specification, except for a couple of zinc content analyses somewhat above the upper specification; see the complaint lot certificates attached as Exhibit 19. I performed no detailed inspection of, say, analytical methods,

manufacturing deviations, exception reports, etc., as these are best pursued at the manufacturing site. Additionally, later review at TUC RP of the numerous documents collected during the inspection revealed some additional questions that I had not noticed or pursued at the time, some concerning the analytical certificates (EX. 19): some concern in-process specifications (bulk analyses) and others concerning product filled into final containers. (Again, these questions might best be pursued at the manufacturing/filling site.) However, as far as zinc assay is concerned, bulk assay results generally should serve as well as final product assay results.

Photocopies of Medwatch reports chosen for further review are attached with the assignment information. They were hard copies which I found at PHX RP, apparently printed previously in anticipation of a possible inspection at Matrixx.

Medwatch # // lot number // product name:

M13919x (legibility problem, x = 3? 8? 9?) (b) (4); nasal gel pump (pump is somewhat like a nasal spray bottle).

M13920x (1? Legibility problem); (b) (4); (b) (4) nasal gel bulk

M139218 (b) (4); nasal gel pump

M139221 (b) (4) nasal gel pump

M139236 (b) (4); C of A for 11838P; nasal gel bulk

M139228 (b) (4); nasal gel pump

Medwatch reports recently received by Matrixx, listed on Matrixx's Exhibits 4 and 5. (Two of these also show up within Exhibits 6 and 7):

M142091 (b) (4); nasal gel pump

M142094 (b) (4) nasal gel bulk

M142097 (b) (4); nasal gel pump

M142106 (b) (4) nasal gel pump

M142536 (b) (4) nasal gel pump

M142709 (b) (4) nasal gel pump

M142887 (b) (4) nasal gel pump

FACTS Consumer Complaint system:

CC 23132 (b) (4) nasal gel pump

CC 29397 (b) (4) nasal gel pump

CC 23857 (b) (4) nasal gel pump

CC 23335 (b) (4) nasal gel pump

CC 23195 (b) (4) nasal gel pump

I also reviewed various printouts, charts, and complaint forms, many printed directly from, or sorted/filtered directly from, the firm's complaint database described above. Because the firm had been working with (b) (4) since only about 11/04, much of the data I reviewed covered the period 11/04 to late May 2005. I focused on data from December 2004; February, March, and April 2005; and some from May 2005. For December 2004 and February / March 2005, I had the firm print copies of all safety complaints for those months. I hand-sorted the anosmia complaints and compared them with various tables/printouts, such as those attached as Exhibits 4, 5, 16, and 17 to look for discrepancies. All anosmia complaint forms for the month of March 2005 are attached as Exhibit 14a.

Additionally, at my request, the firm printed all Forms A for all complaints of any type for all zinc-containing products for April 2005. I did not count the total, but it was obviously hundreds of pages, with firm personnel guessing as many as 900 or so. Without counting, I noticed that a large portion of these complaints forms, apparently more than half,

contained inquiries, not complaints: the firm prints a consumer phone number, a toll-free direct line to (b) (4) on each product carton, and on each container label -- e.g., many forms listed questions about directions for use, the customer having lost both the carton and the insert. Many other complaints are non-safety complaints. Instead of counting/examining forms for all zinc products for the entire month, I selected two groups of 107 forms, from two different places in the several hundred pages (uncounted) of "Cold Remedy" complaint forms, for examination. (b) (4) . I found 14 safety complaints among the 214 total forms. Of these, 5 concern loss of smell/taste to greater or lesser degree. The 9 others are various safety complaints, with burning/stinging the most common. All 14 are attached here as Exhibit 3a.

Mr. Clarot pointed out that as time has gone by, coordination of procedures (etc.) between (b) (4) (b) (4) have improved. Certainly, by the time of the March 2005 data, (March anosmia complaint forms attached as Exhibit 14a), the agreement between data tables such as Exhibit 17a and my actual counts from Exhibit 14a was almost 100%, with any error possibly due to my own counting/sorting method. Overall tabulations and charts produced by Matrixx never show fewer complaints than any counts that I made for any time period.

As written within the Exhibits List, below, for my description of Exhibit 14a: "Drug Product Complaint Forms, March 2005, for safety complaints involving any degree/duration of anosmia. 36, total: I counted/sorted these from a pile of all 148 safety complaints of all types for the entire month of March 2005. A count of anosmia complaints for March from Exhibit 17a yields 38 such complaints, my count of 36 is possibly due to errors in my quick visual/manual sort method."

Overall tabulations and charts never show less than any counts that I made for any time period. Mr. Clarot said that, if anything, Matrixx and (b) (4) are erring on the side of over-counting / over-inclusion when judging safety complaints, and especially anosmia complaints.

Compilations of complaint data provided by Matrixx indicate that some degree of anosmia, of either short or long-duration, is complained of by about 3.6 persons for every 100,000 units sold of the firm's two largest selling nasal zinc products, adult nasal swabs and nasal gel, which together account for about (b) (4) units sold from '99 –'05. The peak rate was about 6.7 per 100,000 during 2004 (which management said was caused primarily by a negative television show during early 2004). Exhibit 17 is particularly useful 'at a glance', and Exhibits 4, 5, 16, 17, 17a, and 18 give the reader an overview of complaint types, trends, by product, etc., for varying time periods.

The (b) (4) source of most anosmia complaints, according to management (both contain zinc compounds) are *Cold Remedy Nasal Gel* and *Cold Remedy Adult Nasal Swabs*, accounting for about (b) (4) units sold and (b) (4) units sold, respectively, since introduction to the market. These are the two products graphed in Exhibit 17, from which the above rates per 100,000 units sold are derived.

Mr. Clarot said that any of the per-100,000 sold (sold, not made) figures given above are barely distinguishable from the "background incidence" of the condition, especially as colds /nasal infections are known to cause anosmia in some people. He said that the firm has contracted for an epidemiological study, the protocol for which is Exhibit 11. He said that the study is largely finished, but has not yet been fully written up, reviewed & approved.

I said to Mr. Clarot that when/if they have large sales figures for their other, non-zinc, nasal allergy or cold products, they should try sorting out anosmia complaints from non-zinc products and see if the anosmia levels are comparable. (I did not attempt to make this comparison myself during the inspection for any samples of the complaints for any given period of time.)

Attached for the reader's information are Exhibits 9, 9a-9d, and 10a-c, which are various items from web searches, press releases, articles, journal publications, etc., concerning various topics: some negative publicity received by the firm's zinc products during early 2004; clinical cold treatment & cold prevention studies; etc.

RECALL PROCEDURES

Due to the focus on complaints and due to time limitations, this area was not inspected.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

The FDA-483:

1) Written procedures describing the handling of complaints are not followed. Specifically: SOP QA-001 (REV # 02, effective date 01/11/05), (b) (4) (b) (4)

However, for product safety complaints, some required information is not found on some forms. More specifically, the provided blank/field, "if no, name of decision maker and date" (concerning the need for investigation of the complaint) is found empty of information on multiple forms marked "no" for February, March, and April of 2005.

DISCUSSION:

NOTE: Due to problems that I encountered with electronic systems such as FACTS & TURBO while preparing the FDA 483 in travel status, the single-item FDA 483 was written by hand, although this report was later prepared in TURBO after resolving the FACTS/TURBO issues. The FDA 483, however, will not be found in the TURBO system.

I presented the FDA 483 to Timothy Clarot, Vice President, Research & Development, during the morning of 5/27/05. Carl J. Johnson, President & CEO, was not available at the time, although I briefly discussed the FDA 483 with him upon his unplanned arrival at Matrixx later in the day.

Earlier, during the course of the inspection, I had discussed any concerns, discussion items, and potential FDA 483 observations with Mr. Clarot and (b) (6), Administrative Assistant to Mr. Clarot. She provided much information on the computer/complaint system and had provided most of the printouts that I reviewed during the inspection.

As can be seen in the discussion below, and within "COMPLAINTS", above, the complaint system review by Mr. Clarot, (b) (6), Ms. Wojcik, and myself was wide-ranging, whereas the FDA 483 focuses on a single item (the SOP and its Form A) and points at one general problem with it ("...some required information is not found on some forms..."). The FDA 483 item goes on to point out one specific example of what is not found: that the name/date of the deciding official are not always given when "investigation required" is marked "no". I said to Mr. Clarot that I planned to use this FDA 483 item as a lead-in to a larger and more widely ranging discussion of the complaint system within the inspection report

Exhibit 1 is the complaint SOP. Exhibit 3 consists of selected examples from all three months mentioned in the FDA 483. The examples include both varieties of Form A. Each type of form is attached as examples for the reader as Exhibit 2. See the explanation of Exhibit 2 in the EXHIBITS list below for important details. (Additional examples of the Form A, which may or may not meet criteria for inclusion on the FDA 483, can also be found in Exhibits 3a, 3b and 14a.) Complaint codes, which appear on one type of Form A, are attached as Exhibit 14.

The complaint procedure (Exhibit 1) is quite clear about the existence of Form A, although no example was attached to the SOP that I reviewed. The two varieties attached to Exhibit 2 were identified to me by Mr. Clarot and (b) (6) as representing Form A. Complaint

data are directly entered into a computer system by (b) (4) employees, and data entry fields as seen on-screen vary in format from the printed versions attached as Exhibit 2. See Exhibit 2a for examples of at least one on-screen view. (I did not determine if other complaint screens are/can be viewed separately from the one depicted in Exhibit 2a.)

When examining the two types of printed forms, one sees that, at two points, questions are asked (i.e., blanks/fields are provided for information) that seem to relate to "investigations", however they might be termed on the forms themselves: Each form has an "Action Required" field, and, farther down the page, an "Investigation Required" field, each requiring a yes or no answer. However, the complaint SOP (b) (4) (b) (4) see section (b) (4) on page 3 of the SOP. (b) (4) (b) (4) (b) (4) (Section (b) (4) on page two of the SOP (b) (4) (b) (4) (b) (4)

Much later, I noticed after the close of the inspection that a thorough examination of the various combinations of answers given in the "action required" field and the "investigation required" field (and the related field for name/date of deciding official) can lead the reader to believe that the name/date are not required, if no investigation is required, if the answer to the PREVIOUS question, "action required", is ALSO "no". There is an overall consistent pattern here, as seen among the various attached Forms A, with a couple of exceptions. However, none of us was able to determine this during the inspection (if indeed my perception described here is correct), and both Mr. Clarot and (b) (6) who reviewed a great many complaint documents with me as I reviewed them, said that there appeared to be no consistent pattern to the use of the field for the name/date of deciding official, and that the deciding official probably should have listed his/her name/date every time "no" was given as an answer to "investigation required".

At various times, speculation was made by both Mr. Clarot and (b) (6) that other answers to other fields found elsewhere on form A might also affect the need for "action", "investigation", or the name/date fields. These included the open/closed status, refund status, etc. However, they said that they were not sure of their guesses. For example, Mr. Clarot stated that there was enough inconsistency in various fields among the various forms examined that he could not be sure what rule(s) the entry operators might be following.

Examples of various combinations of yes/no answers to "action required" , "investigation required" , and name/date of deciding official, as well as forms in which all of these fields are blank, can be found within Exhibit 3b, arranged just for demonstrating various combinations of answers entered by (b) (4) employees. On some forms, attached as Exhibit 3 to demonstrate the FDA 483 item, all of these fields are entirely blank, with no answers to any of these questions, and to some other questions, as well. Mr. Clarot agreed that, whatever the SOP said, and whatever training the (b) (4) & Matrixx personnel might have received, these factors did not appear to be producing consistent results on Form A.

Disjunction between on-screen version(s), two different printed versions, (and, also, perhaps, training instructions given to (b) (4) s staff, but I did not investigate this), could contribute to the lack of specificity in the SOP instructions found, and the resultant variable use of Form A, although this is only a guess on the part of the persons discussing it during the inspection.

Mr. Clarot and (b) (6) said that they will look further into at least two areas, and correct them as needed:

-- Form A: Does it truly serve its intended purposes? Can it be simplified or otherwise modified to minimize entry mistakes?

-- Training: Based upon this FDA 483 item and related observations made during our review of complaints and of the complaint system, re-training of some sort is probably necessary, at least for (b) (4) personnel working on the Matrixx complaints. Training needs will be determined and carried out ASAP.

I also advised them to carefully examine the SOP (EX 1), compare the SOP with actual practices at both Matrixx and (b) (4), with the actual forms used, and where the need is determined by Matrixx, to modify the SOP to describe actual practices more accurately, and with more specificity, i.e., providing less room for interpretation on the part of the reader. Mr. Clarot agreed to do this.

Some days later, in a follow-up telephone conversation with me, Mr. Clarot said that he had nearly completed an extensive revision of the complaint SOP, which he will include with his firm's response to the FDA-483. It will be mailed to LOS DO's District Director and to me upon completion.

REFUSALS

None.

GENERAL DISCUSSION WITH MANAGEMENT

See "COMPLAINTS" and see "OBJECTIONABLE CONDITIONS..." sections, above, for any discussion.

ADDITIONAL INFORMATION

None.

SAMPLES COLLECTED

Sample DOC 86333 of the firm's "Cold Remedy" nasal gel:

Collected for examination of the OTC/homeopathic/drug status of the product, in light of FDA's CPG 7132.15; Homeopathic Pharmacopeia's apparent definition of zincum gluconicum as a Class F solid product, and the HP's monograph for zincum gluconicum. Relevant exhibits, including CPG and monograph, are listed within and attached to the collection report.

EXHIBITS COLLECTED

EXHIBITS, with explanations of some exhibits, as needed:

1 - 3 concern the FDA 483:

1) Complaint SOP.

2) Form A varieties (two printed varieties; they are not as seen on-screen by complaint entry operators at (b) (4).) Related exhibits found later in this list may be of either or both types. (b) (4) (b) (4) The coded variety is used by Matrixx's QA staff and can be accessed/printed by (b) (4) at Matrixx, (b) (6) (See EX. 14 for codes). Both varieties of form are derived from the same source information entered by (b) (4) personnel when complaints are received.

2a) Print examples of on-screen view(s) for complaints at contract complaint organization (Alta).

3) Approximately 25 examples of Form A as described in the FDA 483. (Some may also be found duplicated in other exhibits, such as 3a; 3b; 14a.)

3a) Sampling of safety complaints, anosmia and others, for April 2005, as described below:

At CSO Johnson's request, the firm printed all Forms A for all complaints of any type for all zinc-containing products for April 2005. CSO Johnson did not count the total, but it was obviously hundreds of pages, with firm personnel guessing as many as 900 or so. Without counting, Johnson noticed that a large portion, apparently more than half, of these forms contained inquiries, not complaints: the firm prints a consumer phone number, a toll-free direct line to (b) (4), on each product carton, and on each container label. (E.G. many forms listed questions about directions for use, the customer having lost both the carton and the insert). Instead of counting/examining forms for all zinc products for the entire month, Johnson selected two groups of 107 forms, from two different places in the several hundred pages (uncounted) of "Cold Remedy" complaint forms, for examination. (Cold remedy is the largest seller). He found 14 safety complaints among the 214 total forms. Of these, 5 concern loss of smell/taste to greater or lesser degree. The 9 others are various safety complaints, with burning/stinging the most common. All 14 are attached here as Exhibit 3a.

3b) Examples of Form A, with various yes/no/name & date combinations in the fields "action required" and "investigation required". On some forms, all of these fields are simply blank.

4) Table dated 5/25/05 of Medwatch reports , prepared by Matrixx, concerning anosmia received from FDA for March, April, and May 2005. Table deals largely in product information: lot #, expiration date, manufacturer, assay if performed (or if lot number had been recorded on the complaint), etc. Reports are received from FDA in batches, all dated with same date.

5) Matrixx printout, "2004 FDA Complaint Log". Despite title, log is for the period 2004/2005, and these are actually Medwatch complaints, not other types of complaints such as Consumer Complaints recorded by FDA.

6) Matrixx response letters concerning a batch of Medwatch reports, all dated 4/25/05. Letters include acknowledgement to Medwatch and letters sent by Matrixx to consumers named in the Medwatch reports.

7) DELETED: NO VALUE ADDED TO REPORT: Same as Exhibit 6, but for a batch of Medwatch reports dated 5/17/05.

8) Matrixx letter to Alonza Cruse, District Director, LOS DO, voluntarily sent after negative publicity surrounding Zicam product(s) during early February, 2004. (Matrixx's VP R&D said they had never received any response. Letter does not directly request response)

9) Matrixx website information, some related directly to Exhibit 8 (EX's 9a, 9b), obtained by CSO Johnson 5/19/05:

9a) Press release 2/2/04: "Matrixx Initiatives Reaffirms Safety of Intranasal Zicam ***".

9b) Press release 2/6/04: Update to above press release (EX 9a).

9c) Press release 10/12/04: "Report Underscores Value of Zinc in Treating the Common Cold".

9d) Press release 8/13/03: "Matrixx Initiatives, Inc. Announces New, Improved Swab Design for Zicam **** ; Settlement of Litigation". (Litigation refers to former (b) (4) (b) (4))

10) Three articles, termed reports of clinical studies by Matrixx VP R&D, concerning use of zinc nasal products in treatment & prevention of colds. (Prevention, EX 10c, considers prevention to be ineffective):

10a) ENT JOURNAL, VOL 19 NO. 10, October 2000.

10b) QJM reprint from Volume 96, #1, 2003.

10c) Clinical Infectious Diseases reprint 2001; 33:1865-70.

11) Proposal: A Descriptive Cohort and Case-Control Study of Anosmia. 2/23/04. Study / data said by Matrixx VP R&D to be nearly completed but not yet reviewed/signed.

12) Background information on Matrixx Initiatives Inc:

12a) Miscellaneous web information from Matrixx website and from Yahoo, printed by CSO Johnson o/a 5/19/05, a/o printed by other FDA persons at PHX RP at previous time(s): name change (was Gumtech); company overview; misc product/availability information; management (as of 1/29/04).

12b) Annual report, Matrixx, 2004: selected pages.

12c) Organization chart, May 2005.

12d) FDA drug registration form, submitted 4/14/04. Listed in FACTS as 4/04. Site will update registration.

13) Zicam products list. Zicam is Matrixx's only product line.

14) Codes used on complaints.

14a) Drug Product Complaint Forms, March 2005, for safety complaints involving any degree/duration of anosmia. 36, total: I counted/sorted these from a pile of all 148 safety complaints of all types for the entire month of March 2005. A count of anosmia complaints for March from Exhibit 17a yields 38 such complaints, my count of 36 is possibly due to errors in my quick visual/manual sort method.

15) Examples of anosmia questionnaire forms: new version & obsolete version, with 2 of the 3 examples completed.

16) (b) (4) chart: anosmia complaints, with follow-up, & other information, for all complaints since Matrixx switched to (b) (4) as complaint contractor in November 2004. This chart is produced & updated by the registered nurse at (b) (4), part of a dedicated team assigned only to Matrixx's complaints. This is not the result a computer sort/filter operation. Rather, it is a "cut & paste & type-directly-in" form created outside the computerized complaint system.

17) Graph of anosmia complaints for the (b) (4) zinc products, accounting for almost all such complaints. Part of a presentation prepared by Matrixx for (b) (4) Note that the zigzag graph lines drawn between the numerical figures for each year have no real meaning; the graphed data is only cumulative yearly data, i.e. one data point for each year.

17a) Anosmia complaints by month and year for all products since 1999. Not all products contain zinc, and not all products have been marketed since 1999: years of introduction for each product varied.

18) Chart of complaints of various types, safety and non-safety, including anosmia, for multiple products for April 2005. The overall data are not necessarily useful, according to the Matrixx VP R&D, because a single complaint normally receives multiple complaint codes, causing a single complaint to be listed multiple times in various categories. Therefore, the total numbers are exaggerated on the chart. This appeared to be the case for individual anosmia complaints that CSO Johnson tabulated and then compared with various charts such as Exhibit 17a.

19) Certificates of analysis for multiple lots of zinc containing products. Lots were chosen by CSO Johnson based on Medwatch and/or FDA complaint information, as well as the firm's own Medwatch listing attached as Exhibit 4.

20) Lists of contract manufacturers, packagers, and distribution centers, with lists of bulk/finished products made/packaged by each contract manufacturer.

21) Product specifications/analytical worksheets for various products, analyzed by contract manufacturer and/or their contract laboratories.

22) - 27) Six zinc-containing products: container labels, inserts, outer cartons.

28) Coding: (b) (4) products.

29) Coding: (b) (4) products.

ATTACHMENTS

-- FDA 482's (2):

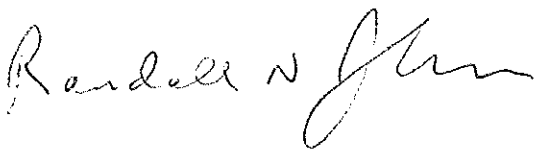
-- (b) (4) 5/24/05 (visited to develop background info on Matrixx)

-- Matrixx Initiatives Inc. 5/25/05

-- FDA 483

-- Sample collection report: DOC 86333

-- Assignment & background information, including selected Medwatch forms.



Randall N. Johnson, Consumer Safety Officer

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 FAIRCHILD, IRVINE, CA 92612 (949) 608 2900	5/25-27/05
	FEI NUMBER 3004456620

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: TIMOTHY L. CLAROT, VICE PRESIDENT RESEARCH + DEVELOPMENT

FIRM NAME	STREET ADDRESS
MATRIXX INITIATIVES INC.	4742 N. 24th ST SUITE 455
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
PHOENIX, AZ 85016	OWN LABEL DISTRIBUTOR

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

(1) WRITTEN PROCEDURES DESCRIBING THE HANDLING OF COMPLAINTS ARE NOT FOLLOWED. SPECIFICALLY:

SOP QA-001 (REV # 02, EFFECTIVE DATE 01/11/05), (b) (4)

(b) (4)

(b) (4) HOWEVER, FOR PRODUCT SAFETY COMPLAINTS, SOME REQUIRED INFORMATION IS NOT FOUND ON SOME FORMS. MORE SPECIFICALLY, THE PROVIDED BLANK/FIELD, "IF NO, NAME OF DECISION MAKER AND DATE" (CONCERNING THE NEED FOR INVESTIGATION OF THE COMPLAINT) IS FOUND EMPTY OF INFORMATION ON MULTIPLE FORMS MARKED "NO" FOR FEBRUARY, MARCH, AND APRIL OF 2005.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Randall N	CONSUMER SAFETY OFFICER	5/27/05