I started here at the Portage site with The Upjohn Company in 1980 as an analytical chemist and retired in October 2017 after 37 years. Today I want to show you that this site has a lot of special history.

- <u>Timeline of the Portage Site</u> Here are the company names associated with the Portage Site. Pfizer has owned the site for the last 16 years.
- <u>WE Upjohn</u> William Erasmus Upjohn, better known to us as WE Upjohn, was born in Richland during 1853. He was awarded a medical degree at the University of Michigan in 1875 and became a country physician, based in Hastings. He moved to Kalamazoo in 1887. W.E.Upjohn has the distinction of being the very first person in Kalamazoo County to drive an automobile and here it is. I'm sure it was a very rough ride back then on dirt roads intended for horses.
- Friable Pill Pills in that era were so hard they usually travelled right through the patient without dissolving. This is because clay was usually used as the binder and clay gets harder over time. You could take a hammer and pound these pills into a plank of pine wood and they would not break. Obviously, the efficacy for the patient was zero. This situation really bothered W.E.Upjohn and he started experimenting with ways to create a pill that would dissolve within the body. He became quite obsessed with this and one day he succeeded.
- The Upjohn Pill and Granule Company began in 1886 in Hastings. The three principals were brothers W.E.Upjohn, Henry Upjohn and James Upjohn and their innovative product was the friable pill. The word friable means easily crumbled into smaller particles. The new company used a logo of a thumb crushing a pill and this remained part of the logo for 60 years.
- <u>First Building</u> The Upjohn brothers wanted to build a factory in Hastings but the city council there would not allow it so The Upjohn Pill and Granule Company moved to Downtown Kalamazoo. Kalamazoo had a population of

14,000 people at that time and called itself the "Windmill capital of the world". It was also a leader in buggy manufacturing – 47,000 buggies had been made. The first Upjohn building was on Farmers Alley, which is one street south from the current Downtown Mall.

- <u>First Price List</u> Here is the first Upjohn price list in 1886. It was one large page that listed 110 different pills and 50 granules. Those are impressive numbers for a brand-new pharmaceutical company.
- Upjohn Products Contained here are some interesting active ingredients in those 1886 products. What they all have in common is they come from natural sources, either plant extracts or minerals. They were no chemical or biological syntheses back then. None. There was no chemical or biological testing either. When active ingredients arrived at the company, the three tests performed on each batch were (1) Does it look the same as the last shipment; (2) Does it smell the same; and (3) Does it taste the same. That was it!
- <u>Early Expansion</u> With pills that actually dissolved in the body, Upjohn became very successful. By 1904 the company price list was 192 pages long. More buildings in Downtown Kalamazoo were either bought or built by the company. Building 19 shown here was purchased in 1926 from the American Playing Card Company. The road in front of Building 20 is the current South St. In front of Building 19 is the long-gone Taylor St.

<u>Manufacturing Complex</u> - Eventually the Upjohn triangle was formed downtown, which was all the land between Lovell St, South St and Portage Rd. This included a company power plant. All the buildings shown here are Upjohn buildings.

During the Great Depression (1929-1939) W.E. Upjohn did not lay off any of his workers. He formed the Upjohn Farms in Richland at that time. Upjohn employees not needed for manufacturing worked at the farms to cultivate

vegetables and fruit, which were then sold in Kalamazoo. Because of The Upjohn Company and the many paper mills in the county, Kalamazoo came through the Great Depression very easily.

- <u>Major New Buildings</u> Shown here are the production tower, Building 25, and the headquarters building in front of it, Building 24, were both built in 1934-5. These were major buildings and both were paid for entirely out of earnings. No loans were needed. That tells you how successful the company was. B25 was demolished in 2007 and B24 is now used by Bronson Hospital. Do you see The Upjohn Company spelled at the top of the building? That's still there today.
- <u>Late 1930s Production</u> However, you can see from this late 1930s photo, production in the tower during that era was cramped. During WWII it became obvious the company needed a major expansion of manufacturing facilities. Company leaders considered building upwards in Downtown Kalamazoo but decided to buy a spacious site outside the city.
- <u>Building of the Portage Site (7 slides)</u> In 1946 1,500 acres of land were bought on Portage Road, the location of our current manufacturing site. At the time the city of Kalamazoo stopped at Cork St and there was no city of Portage, just Portage Township. On postcards from that era the new site is described as being near Vicksburg.

This is the first conceptual drawing of the buildings on the site. Construction started in 1946 and it took 5 years to complete it. It cost \$32 million to build the entire site, all paid for out of earnings. No loans needed. Building 38 opened in 1948 and the site was fully opened by April 1951, so we have been manufacturing here for 71 years.

• <u>Grinding Adrenal Glands</u> – the Portage site was now in operation but chemical synthesis was not here yet. In the early 1950s here we have an Upjohn employee in Building 39 grinding adrenal glands from cows. This

was the first step in extracting cortisone from them. It took a lot of glands to make a little cortisone and the final product was very expensive. I can't help but wonder how bad this grinding operation smelled. I'm pretty sure the newest employee got this job.

However, during the 1950s Upjohn brought in chemical syntheses and biological fermentations on a large scale. This was truly a revolutionary advance. Suddenly, steroids could be made in large amounts at low cost. For the first time, patients could afford them. By 1960 the big products of the company at this time were steroids like cortisone, progesterone, methyl-prednisolone, prednisone and hydrocortisone. It also made antibiotics like neomycin, streptomycin and lincomycin. Business was booming. BTW, we started making Gelfoam in 1946, Heparin in 1950 and Solu-Medrol in 1957.

- <u>Upjohn Buses</u> every employee at the new Portage plant lived in the City of Kalamazoo, which stopped at Cork St, and not everyone had an automobile back then. Thus, the company bought buses to shuttle people from Kalamazoo to work at the new plant in Portage. The fleet of Upjohn buses eventually grew to 15.
- **Barbers Shop** Because the Portage Site was so far from the city, a barbers shop, a pharmacy and a check cashing service were provided on site. All three of these lasted into the 1980s and I can remember using them. I got my hair cut in the basement of Building 41. That barbers shop is now the Training Track room.
- <u>The Upjohn Airforce</u> in 1956 Upjohn bought their first plane and build a company hanger at the Kalamazoo Airport. The goal was to fly executives and high-level employees around the country as needed. In 1959 a Grumman Gulfstream that held 16 passengers was added. By the mid-1980s there were 4 planes and 7 pilots. 1100 employees per month used the planes. Everyone called it the "Upjohn Airforce".

- <u>Upjohn Awards</u> When W.E.Upjohn died in 1932, he set aside a large block of Upjohn stock to fund an annual award for employees. These were the Upjohn Awards. It truly was an honor and the high-point of a career to get one. In the 1980s there were 40 to 50 awards made each year, and each recipient would have received a check for as much as 7 thousand dollars.
- Public Tours From 1960 to 1989 there were organized tours of Building 41 that the public could take. Tour participants started in a museum at the west end of the basement (right next to the concourse), climbed to the first floor and walked to the East end through manufacturing, then returned to the museum via the basement. They viewed sterile filling, tablet compressing, fluid production, packaging, sterile inspection and all the supporting shops. Participants ended up in the cafeteria for refreshments. These tours were very popular. Busloads of people arrived daily to take a tour and part of orientation for new employees was taking a tour. The top photo is of the tour guides in the mid-1960s.
- <u>Centenary in 1986</u> The centenary of The Upjohn Company was in 1986. There were 19 nights of parties for employees at the Hilton Hotel in Downtown Kalamazoo. The Hilton later became the Radisson. At this time, the definitive book on The Upjohn Company "A Century of Caring" was published. Nine years later in 1995 The Upjohn Company ended when it merged with Pharmacia to form Pharmacia & Upjohn.

Now let's take a look at some of Upjohn's more unusual products

 <u>Blue Mass</u> - Mercury has been used by humans for thousands of years. Medically, it was used to treat syphilis, typhoid fever, yellow fever, parasites, constipation, mental health conditions and others. From the 17th to the 20th century, a mercury formulation called Blue Mass was sold throughout the country. It was taken in either pill or syrup form.

Many companies and formularies made Blue Mass pills and syrup. Here is an Upjohn bottle from the 1890s. Read from slide. This particular product was made by Upjohn from 1886 to 1925. A 39-year lifespan indicates this was a good seller for the company.

It's well-known that Abraham Lincoln took Blue Mass pills for several years to treat what was then called melancholy. Today we would call this depression. However, when taking Blue Mass, he was prone to erratic behavior and violent outbursts. He recognized this and stopped taking the pills, which was a good thing. Nobody wants a president prone to erratic behavior and outbursts.

- <u>Mercury Ointments</u> Mercury was also formulated in ointments for rubbing onto the skin and here are a few examples. Note the top tube contains 30% mercury. These were used to soothe skin irritations such as eczema, psoriasis, impetigo, also sores caused by syphilis and herpes viruses. In 1890, Upjohn offered 16 different ointments containing mercury, the highest level of mercury being 50%.
- <u>Corrective Infants</u> Mercury wasn't just for adults. Oh no! It was given to infants too, as shown here. The term Corrective on the bottle simply means correcting a health problem. Mercury was used for infant teething pain also. Hopefully those infants got over their problems quickly before

mercury poisoning hit them.

I looked through an 1890 Upjohn catalog and found 43 products containing mercury, the amount of mercury ranging from 1/1000 of a grain to 5 grains. A couple of interesting combinations were mercury and opium, and mercury and rhubarb extract. In a 1942 Upjohn catalog, there were 62 mercury-containing products. Thankfully by 1960 there were none.

 Quinine pills – Quinine used to be the first choice for treating malaria, which is a bad fever caused by the bite of a mosquito that has the disease. Quinine pills were huge sellers for the Upjohn Company and many other companies too. At one point, quinine pills were 40% of total Upjohn sales. They sold so much, Upjohn was known as the quinine company.

In the 1800s, almost everyone in Michigan had malaria because of all the wetlands in the state. It was said on the East Coast at that time "Don't go to Michigan, that land of ills, the word Michigan means aches, fever and chills." It was not until most of the wetlands were drained that malaria was no longer seen in Michigan.

Malaria was a world-wide problem at that time, making quinine pills a global seller. Every explorer heading out to Africa, Asia or South America was sure to take a good supply of these pills. The metal cases helped to securely transport the pills across rough country.

Upjohn sold 65 different formulations of quinine pills and tablets between 1895 to 1949. However, quinine has some serious side effects so it's now the third-choice option for treating malaria.

<u>Creosote</u> – Many of us know creosote as the substance that you paint fence posts and outdoor wood with, so the wood is protected from the weather. It's nasty, smelly stuff. That creosote is made from petroleum products. Upjohn sold pills containing creosote made from beach wood. Guess what?
it's still nasty and smelly. So why would people choke down creosote pills?

Actually, it's an effective treatment for diarrhea and stomach aches. It's carbon and carbon absorbs.

The Creosote product on the left was made by Upjohn between 1888 and 1929. This particular bottle was filled before 1902, and I can say that because it has the original name of the company on it. On the right, Creosotone is an Upjohn product name. I'm guessing this bottle was filled in the 1930s or 1940s. I'm just thankful that in 2019 I don't have to swallow creosote for an upset stomach.

- <u>Hematic tonic</u> here's one of my favorites. A tonic is supposed to perk you up, right? Note three of the ingredients in these pills arsenous acid, mercuric chloride and strychnine sulfate. So this tonic contained arsenic, mercury and strychnine. Wow. Why would anybody make this or take this? Well, there used to be a homeopathic principle that a very small quantity of poison will really perk up your system. There was no clinical testing and there was no FDA to regulate products back then so companies could sell anything they wanted. It didn't matter if a product worked or not, or how toxic it was to the patient. There were no rules at all until 1906 when the Pure Food and Drugs Act was enacted. However, FDA in its current form did not exist until 1920 and only then was there a real push to eliminate all the harmful products and products that had no therapeutic effect.
- <u>Aphrodisiac</u> Now let's talk about love. Upjohn sold these Aphrodisiac pills from 1886 to 1933. The batch number of 28307 on the lower right of the bottle label dates this one to 1916. Damiana is a wild shrub that grows in Mexico, Central America, and the West Indies. The leaf and stem are both used in tablets and are said to increase sexual desire. However, we have no scientific proof that it works for this.

Does anyone know the better-known name for Cantharides? It is the famous Spanish Fly, which was in use as far back as the Romans 2,000 years ago. Spanish Fly is made from crushed blister beetles and this substance causes an inflammation of the genital organs. It actually does work but the

inflammation can be painful and the dose needed to cause it is close to being fatal. Used over time it will cause liver and kidney damage. So yes, the price of love can be very high.

Interestingly, at the very end of The Upjohn Company, a product called Caverject was approved by FDA in July 1995 for erectile dysfunction. Caverject contains Alprostadil, also known as Prostaglandin E1. Alprostadil acts as a vasodilator, allowing more blood to rush to the penis. It does require an injection with a small needle but it works. Even in the era of Viagra and Cialis, Pfizer still sells this former Upjohn product today. Think of it as a modern version of Cupid's arrow.

<u>Cannabis</u> - Cannabis, also known as marijuana, was a very popular medication in the 19th and early 20th centuries, and every pharmaceutical company sold it. This particular Upjohn product was made from 1900 to 1931. From the batch number of 47092 I would date this bottle to the early 1920s. It was originally in the collection of a country doctor. When that doctor died 5 years ago his family auctioned it on eBay and I really wanted it for my own Upjohn bottle collection. I bid \$100 for it but it sold for \$450. Historic cannabis items are all very collectable.

So, would the cannabis in those pills still be enjoyable? As you already know, it would be far too risky to take any. A hundred years of degradation has likely produced some toxic impurities inside these pills.

- <u>Cocaine, Heroin, Opium and Morphine</u> Cocaine, heroin, opium and morphine were also well-known and popular pharmaceuticals in the 19th and early 20th centuries. Every pharmaceutical company made them because they were so profitable. Upjohn made all of them. Upjohn morphine products lasted until the late 1970s. These were all very addictive substances of course but back in the day nobody worried about that.
- Here are some old advertisements to prove my point. Cocaine was good for toothache. Heroin for good for coughs. Opium could be used to get a good

night's sleep. Mrs. Winslow's Soothing Syrup contained 65mg of morphine per fluid ounce. It was advertised as providing relief for children who were teething but in 1911 The American Medical Association denounced the syrup as a "baby killer". Despite this, it remained on sale for another 10 years.

- <u>Chocolate Coated Tablets</u> Cascara Sagrada, often shortened to Cascara, is a large shrub or small tree. Its bark has laxative properties and it's helpful with chronic constipation. Perhaps that's why the Indian name translates to "Sacred Bark". When dried and aged the bark can be included in a tablet. Upjohn sold such tablets from 1900 to 1929. Cascara does have a very bitter taste and so Upjohn coated these with chocolate. Both coated and uncoated tablets were sold so the chocolate-coated tablets were likely for use by children.
- <u>Creosote and lodine Tablets</u> Upjohn did chocolate-coat other products, such as these creosote and iodine tablets. This product was made from 1905 to 1946. Again, the chocolate coating was probably intended for children. Can you imagine giving your kids creosote and iodine? It amazes me how well the chocolate coating has lasted. This bottle is at least 70 years old but the chocolate looks to be in perfect condition.
- Pantomime Candies Upjohn's entrance into the world of candies was done with the help of noted Kalamazoo candy maker Bert Kitchen in late 1920. The box was colored a rich brown and shows a group of partiers. I'm not aware of any of these boxes having survived. Alas, only one batch of Pantomime Candies was ever made in the Upjohn factory. The chocolates were said to be tasty but had a hint of "pharmaceutical odor". The project was promptly cancelled and the 800 pounds of chocolates created never made it to store shelves. They were instead given to employees on May 6th 1921 to celebrate the birth of a daughter to company treasurer John S. McColl.

- <u>Wound Tablets</u> Upjohn wound tablets were manufactured for the troops in World War II. They contained sulfadiazine, which is a sulfonamide antibiotic effective against most gram-positive and many gram-negative organisms. This was truly ground-breaking. Use of the sulfonamide antibiotics was a huge improvement in wound care. You can see that inside the package was a hard-plastic container with 8 tablets. Soldiers carried them in a pocket and if they were injured, they crushed one or more tablets and dropped them into the open wound. Believe it or not, this was state of the art medical treatment at that time, which is only 80 years ago. Upjohn made these wound tablets from 1942 to 1950.
- <u>Vanilla</u> This is a unique Upjohn product. It was only for sale to company employees. The story I was told was that Martha Parfet, wife of 1970s Upjohn CEO Ted Parfet, used a lot of vanilla in her cooking but could never find a good quality source of it in town. You know that saying "Happy wife, happy life"? Ted needed to do something and since The Upjohn Company already used large quantities of vanilla-flavoring in products like Kaopectate, the materials were already in-house. It didn't take much effort to formulate and bottle it. This Vanilla product was made available to all employees across the world. It really was a popular product because batches were made through the 1970s and 80s. It was discontinued in 1990.
- <u>Rennet</u> Here's a more recent unusual product. Rennet is an enzyme used to coagulate milk in order to form a thick curd. It is used primarily in cheese-making. A maker of kosha cheese products in Wisconsin contracted with Upjohn in the 1990s to produce rennet by fermentation at the Portage plant. Before any batches were made, a rabbi arrived on site to kosher-certify all the fermentation equipment and all the ingredients used. A tanker truck was driven down from Wisconsin to pick up each batch of kosher rennet. This contract lasted for 2 years.

- <u>Consumer Products</u> In the 1980s the consumer products some of you may remember seeing in your parents or grandparents houses were still being made here in Portage – Kaopectate, Mycitracin, Unicap, Cheracol, Cortaid, Motrin and Pyroxate.
- <u>Rogaine</u> I'm going to end with Rogaine. The active ingredient in Rogaine is Minoxidil, which was originally used to treat hypertension. Surprise – those hypertensive patients started growing hair and The Upjohn Company took notice. It was claimed at the time that 35 million men and 20 million women in the US were losing their hair, a huge market to sell to. Some analysts believed that Rogaine could be one of the biggest selling drugs ever.

It became available for men in 1988 and for women in 1992, both by prescription. In 1996 Rogaine was made available over-the-counter, so no prescription was needed anymore. Alas, it never became a true blockbuster product and in 2006 Pfizer sold Rogaine to Johnson & Johnson.

Everything I've shown you is on the website <u>www.upjohn.net</u>. This site has 800 web pages, over 15,000 images and 19 videos. Anyone in the world who can access the internet can see it and I'm always adding more information to it. Any questions?

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