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"Drug Delivery Devices- Using Nano-Positional Accuracy"

Many drug delivery devices are now manufactured in non-traditional ways such as silicon wafer technology, MEMS, and ground-up manufacturing methods. These methods are then matched to more traditional top down methods to provide medical and pharmaceutical companies with differentiated and strategic value. These processing techniques are typically developed using "conventional" single micron level positional accuracy using current work holding devices. These methods are inadequate in preventing cross contamination of actives in capillaries and other microscopic microfluidic assemblies. This article explores ground-breaking nano-positioning methods for producing 25-100 ***NANO***meter tolerances of seal to vessel, lid to chip, or sub-component to sub-component.

NANOmeter-positional accuracy? Really? This was absurd to even dream about only a few years ago. Even today, traditional pallet-holders coupled with automatic X, Y, Z probing can barely guarantee a 1 MICRON positional accuracy. It is also strange to think in a completely different dimension, orders of magnitude smaller than can be seen with a microscope. It is evident, however that developing drug delivery devices require thinking like the human body thinks and the human body thinks in nanometers and less. White and Red blood cells on average range from 8-100 microns in diameter and DNA can be as small as 2-3 NANOmeters. In between these two range a great deal of discovery and science that we cannot begin to understand without simulation outside the body and mimicking strands of DNA and blood cells working together. It is for this reason that drug delivery and medical and pharmaceutical device companies are looking for help from manufacturers to push the envelope and think out of the box to achieve features and tolerances in the NANOmeter range. What we have discovered in the micron range has certainly helped us to learn some top down methods that didn't work and some bottom up methods that worked (see Figure 1.1) but needed some refinement using an in between top/bottom method.

"Top Down" Methods	"Bottom Up" Methods
Laser Machining	Genetic Code
EDM-WEDM	Complexity Theory
Ultrasonic Machining	Self-assembly
Ion Machining	Biological Cell
Grinding	Proteins
CNC Machining	DNA and RNA
Chemical Milling	LIGA
Photochemical Milling	
Electrochemical Machining	

Figure 1.1: MES Micro and Nano Manufacturing Methods Used today and in the future

Growing molecules (Bottom Up) methods to create geometry is not something we micro peeps like to think about let alone manufacture. We will force that top down methodology until we can mill, grind, edm, diamond turn, and etch no more. But at some point in the near future, we will all be looking to at least LIGA as well as different tool-holding mechanisms to create geometry, surfaces, and parts beyond our capabilities in Top-Down Methods employed today.

For developing parts with features and tolerances to the singular microns, pallet holders are common tools used to hold and manufacture molds, tooling, fixtures, and components. These can possibly be dialed in to nearly +/- 2 microns using ultra-precision touch probes in temperature and humidity controlled manufacturing environments. To get the NANOmeter positional accuracy, however conventional equipment and work-holding pallets cannot be used. As is the case with chasing micron and nanometer tolerances, manufacturers must develop their own methods, fixtures, tooling, and equipment to do the job. Every work holding fixture and automation end of arm tool is customized for picking and placing dust-specked size parts and smaller.

Other drug delivery devices that are enabled by nanometer positional accuracy:

- Powder Inhaler Mechanisms
- Microfluidic Chip/Cover Assemblies
- Intraocular Implant Surfaces
- Insulin Delivery Pumps
- Bio-Resorbable Polymer Thin walled Implants
- Surface Coating/Masking
- Elusive "Flash-less" Molding

One of the products most often common and challenging to our micron to nanometer tolerances are microfluidic chips and covering them with a polymer, adhesive, or membrane lid. Average microfluidic channels are less than 100 microns in width (See Figure 1.2) so they can carry red and white blood cells or other fluids without blocking the channels. The velocity by which the capillary action works makes no room for error, which means no room for channel to channel cross contamination. The lid or cover must be held in place sometimes on a shelf as small as 10 microns in width. This thin surface area is challenging to accurately position a piece of thin polymer, adhesive, or membrane to seal the channels and keep them from leaking into one another. This is a catastrophic failure for critical tests such as HIV, TB, or Malaria, to name a few.

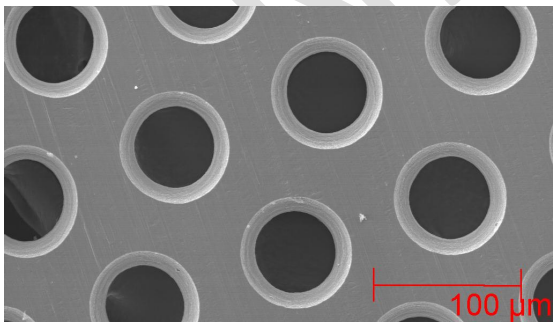

Figure 1.2: MES SEM Image of Microfluidic Device

Another worldwide challenge for wireless drug delivery devices are MT Ferrules used to generate light and bandwidth for wireless devices. These devices have two 600 micron holes with ten to twelve 125 micron holes between them. (See Figure 1.3). The very best that can be done using conventional pallet holders is +/- 2 microns as a stack-up tolerance device. With customized nanometer positional assembly holders, this MT Ferrule can be made to 100 NANOmeter

positional-accuracy. This leads to an overall product improvement of 15-25% additional light or bandwidth, which can send data faster than ever before to wireless devices (See Figure 1.4) so common to many physicians, researchers, and engineers developing drug delivery devices of the future.

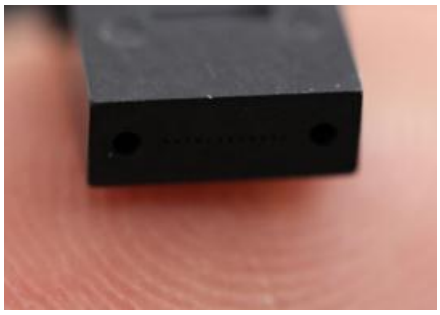

Figure 1.3: MES MT Ferrule Image on a Fingerprint. (Two 600 um holes and twelve 125 um holes shown on face)

Figure 1.4: MES Photo showing Wireless Devices of the Future using CT Scanning for exact CAD modeling

Measuring parts such as the MT Ferrule and other wireless devices that are trending to nanometer positional accuracy is also spurring new metrology equipment such as CT Scanning to measure parts accurately and in ONE SETUP, an absolute critical factor in reducing error in any tiny part or feature manufacturing process. CT Scanning can scan a 2d or 3d component or assembly from a top down view and create a point cloud of data which can then be compared to a nominal solid model. This powerful tool saves countless hours of picking up a part in several planes, creating multiple fixtures to effectively "show" the part to the correct lighting beam, and then repeating this process for each plane required. Again, each time that part is picked up and placed down, another datum plane is required that may or may not be able to link to the previous datum. This can be a challenging and error-prone "stitching" process.

Non-traditional methods for manufacturing such as nanometer positional accuracy and dust-specked sized injection molded, machined, and assembled components are spawning many new products for drug delivery device companies. These new methods combine traditional top down methods and futuristic bottom up methods to provide medical and pharmaceutical device companies with enabling products to treat the likes of diabetes, glaucoma, and third world country vaccination to name just a few. We are fortunate as micro and nano manufacturers as we play a part in enabling these treatments and products that contribute to worldwide health.

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