DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

SEP 1 8 1998

Docket Number: 96P-0444

Mr. Stephen M. Dolle
13191 Gwyneth Drive #A
Tustin, California 92780

Dear Mr. Dolle:

This letter is in response to your Citizen's Petition of November 6, 1996. In your petition, you requested the Food and Drug Administration (FDA) take action concerning Pudenz Schulte Medical Research Corporation (PS Medical) for its Central Nervous System (CNS) Delta Shunt with Siphon Control Device (SCD) and action concerning Heyer Schulte NeuroCare, L.P. for its Anti-siphon Device (ASD). Specifically, you requested FDA to: (1) require changes in manufacturers' labeling, (2) require a new package insert to warn of adverse events, (3) require manufacturers to conduct testing for adverse events under conditions of normal sleep and external pressure and make the results available to physicians and patients, (4) require the surgical section of the manufacturers' labeling to describe the adverse events, (5) inform all U.S. neurosurgeons and neurologists about the new warnings and labeling changes, (6) inform all other U.S. professionals through the FDA Medical Bulletin about the new warnings and labeling changes, and (7) impose restrictions in the use of these devices.

Based on our evaluation of your petition, the medical literature, and adverse effect reporting to the agency, we are in part granting your request (1), (2) and (4) relating to device labeling as indicated above. While it is not feasible at this time for FDA to mandate specific wording in the labeling of each of these devices, there is a long-standing statutory obligation on the part of the manufacturers to provide adequate information in labeling regarding the safe use of their products. This includes a description of the known risks to health from the use of the device. We have met with CNS shunt manufacturers to review their current labeling and directed them to re-evaluate their labeling to include appropriate warnings of adverse events. In response to (5) and (6), we are moving forward to have a broader evaluation of shunt devices in a public forum to see if any further public and/or health care provider notification is necessary. We intend to work closely with the medical device industry, the medical community, and consumers to address the public health issues that exist with CNS shunts.

SEP 18 1998

The agency is denying parts (4) and (7) of your petition. First, there is insufficient evidence to require CNS shunt manufacturers to conduct specific device testing at this time and to restrict the use of these devices. Secondly, there is no validated test method to simulate the failure modes you described. However, our Office of Science and Technology is reviewing current test methods and assessing an in vitro model to more rigorously test shunts and their components. Should this evaluation lead to the identification and validation of new methods which would increase the assurance of the safety of these devices, we would share them with the manufacturers, the public and work diligently to have them included in the consensus standard being developed for central nervous system shunts.

While we are unable to grant your petition in full at this time, we remain committed to following the issues that you raised and would greatly appreciate your continuing to share information on this subject with the agency. If you have any additional questions concerning this letter, please do not hesitate to call Mr. James Dillard, Deputy Director, Division of General and Restorative Devices, Office of Device Evaluation, at (301) 594-1184.

Sincerely yours,

D. Bruce Burlington, M.D.
Director
Center for Devices and
Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAY 30 1997

Stephen M. Dolle
13191 Gwyneth Drive #A
Tustin, California 92780

2137 '97 JUL 24 A9:22

Re: Citizen Petition,
Docket Number 96P-0444/CP 1

Dear Mr. Dolle:

This letter is to inform you of the status of your citizen petition dated November 6, 1996, and filed by the Dockets Management Branch on November 15, 1996. Your petition requests that the Food and Drug Administration, among other things, require a change in manufacturers' labeling and warnings of CNS Delta, siphon-control device (SCD) and anti-siphon device (ASD) shunts.

Because of the scientific issues involved and limited resources, we have not completed our review and evaluation of the labeling and adverse data relating to these devices as suggested by you. As soon as our review is complete, we will issue a response to your petition. Please be assured the agency is fully committed to considering your concerns.

If you have any questions, please contact Thomas Callahan, Ph.D., on 301-443-8320.

Sincerely yours,

Joseph A. Levitt
Deputy Director for
Regulations
Center for Devices and
Radiological Health

96P-0444

LET2

NOTE TO: HFA-305

FROM: Regulations Staff, HFZ-215, OHIP, CDRH

DATE: July 18, 1997

Subject: Citizen Petition
Docket Number 96-0444/CP 1

Please place the attached response in the above cited docket. Any questions, I can be reached on 301-827-2969 or e-mail JXW.

Thanks,
Jennette Wade

STEPHEN M. DOLLE
3191 Gwyneth Drive #A
Tustin, CA 92780
(714) 669-9991

April 25, 1997

Dockets Management Branch
Food and Drug Administration, Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

ADDENDUM OF ADDITIONAL ADVERSE SAFETY AND EFFECTIVENESS TO CITIZENS'S PETITION ON CNS DELTA AND ANTI-SIPHON SHUNTS; FILED NOV. 15, 1996, DOCKET #96P-0444/CP 1.

Dear FDA Staff:

Let this correspondence serve as an "addendum" to the safety and effectiveness concerns in the above-noted Petition. This is also a new summary of the safety issues. I urge you to take action on this Petition, and further, to ascertain how these safety issues existed unabated for 15 years. The six-month petition ruling period will expire on May 15, 1997.

CNS Delta shunts (Medtronic/PS Medical) and their counterpart anti-siphon devices (Heyer-Schulte) are described in medical studies to experience unpredictable shunt insufficiency, more associated with the upright posture, and quite difficult to detect. These reports are described separately by field neurosurgeons Higashi, Chiba, Drake, and Aschoff in studies. Their combined studies identify four (4) adverse safety and effectiveness factors impacting anti-siphon shunt performance not identified in the product labeling, described as:

1) The shunt upright opening pressure is dependant upon the length of the distal catheter which is calibrated to be between 50 and 80 cm. of length. A length longer than 70 or 80 cm, as in a tall child or adult, can cause an SCD (siphon control device) or ASD (anti-siphon device), distributed by the above two manufacturer's, respectively, to overfunction and cause harmfully increased intracranial pressures (ICP) in the upright posture.

2) The functional opening pressures and operation of these devices in the upright posture is very dependant upon a theoretical vertical implantation site relative to a horizontal plane through the foramen of Monro. However, studies have confirmed that no such theoretical site exists at this location, and that this site adds 10 cm. or more to the upright opening pressure. The true site is said to be some 10 cm. below this point, possibly extending into the soft tissues of the neck, a place contraindicated and certainly not advocated for integral anti-siphon shunts. Implantation sites above the calibrated site causes an overfunctioning of the shunt with harmfully increased (ICP) in the upright posture.

It is postulated there is a 1 cm H2O change in opening pressure for each 1 cm of distance above this new calibration point. The implantation site may also be complicated by an existing high frontal ventricular catheter. Implanting of integral Delta and Heyer-Schulte anti-siphon shunts adjacent to a high frontal catheter will abnormally raise the shunt's upright opening pressure. Revising to an integral anti-siphon shunt here will alter SCD/ASD function and pressure model selection, particularly in tall children and adults. These changes in opening pressure are more dramatic in patients with low to medium pressure requirements.

3) and 4) The operation of these devices is very dependant on its ability to "measure" true atmospheric pressure which it uses as a reference point via a sensor in the shunt under the scalp. The shunt in this way controls opening pressure, which controls the patient's subsequent CSF (cerebrospinal fluid) flow and ICP. Research now indicates that overlying scalp involves a variable amount of pressure on the sensing mechanism, described as indeterminate from site to site. This additional pressure causes the devices to overfunction and cause harmfully increased (ICP) in the upright posture. The increase in opening pressure is said to be equal to the increase in overlying scalp pressure. It presents a diagnostic dilemma to neurosurgeons and patients. It is described to be more problematic in the upright posture.

The presence of average pressures generated by lying on a pillow during sleep also abnormally raise the shunt's opening pressure and patient's resulting ICP. This is described by Aschoff and Drake as a mechanical liability. It is not identified in the labeling.

My experience with my own integral anti-siphon (Delta) shunt, attached immediately adjacent to a frontal ventricular catheter, has found that tightening of facial musculature during normal facial expression produces tightening of the scalp overlying the shunt, and retards its function.

Paradoxically, a decrease in external pressure such as from a low pressure storm front, or a stay in the mountains, does lower the shunt's opening pressure, and ICP. This may present a problem for a patient shunted at one geographic elevation, then later moving to another substantially higher or lower elevation.

The Petition presented field evidence that the two noted manufacturers were aware of adverse reports and design difficulties, but refuted the studies for many years. The adverse findings are reported to occur in a manner often undetectable by routine diagnostic and clinical assessment. In consideration, I believe this creates some urgency for FDA action on the Petition, and an inquiry to the under-reporting of these complications. I am in the middle of research into a new method of evaluating shunt complications, including those of anti-siphon devices. I will make this available when the opportunity permits.

CERTIFICATION

I, the undersigned, certify that to the best knowledge and belief, this addendum to the noted Petition includes representative data and information which is true and in consideration of facts which are also adverse to the petition.

Dated: 4/25/97

By: Stephen M. Dolle

Stephen M. Dolle
Hydrocephalus Researcher
13191 Gwyneth Drive #A
Tustin, CA 92780
(714) 669-9991

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

November 18, 1996

Stephen M. Dolle
13191 Gwyneth Drive #A
Tustin, CA 92780

Dear Mr. Dolle:

Your petition requesting the Food and Drug Administration to make immediate changes in manufacturers' labeling and warnings of CNS Delta, SCD, and ASD shunts, to post immediate warnings to all users, and restrictions in its use was received by this office on November 15, 1996. It was assigned docket number 96P-0444/CP 1 and it was filed on November 15, 1996. Please refer to this docket number in future correspondence on this subject with the Agency.

Please note that the acceptance of the petition for filing is a procedural matter in that it in no way reflects an agency decision on the substantive merits of the petition.

Sincerely,

Lyle D. Jaffe
Dockets Management Branch

STEPHEN M. DOLLE
13191 Gwyneth Drive #A
Tustin, CA 92780
(714) 669-9991

November 6, 1996

Dockets Management Branch
Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

CITIZENS'S PETITION TO REQUIRE CHANGE IN MANUFACTURERS' LABELING AND WARNINGS OF CNS DELTA, SCD, AND ASD SHUNTS, TO POST IMMEDIATE WARNINGS TO ALL USERS, AND RESTRICTIONS IN ITS USE.

To FDA Staff:

I am writing to request that you immediately take action against Pudenz Schulte Medical Research Corporation (PS Medical) for withholding safety and effectiveness (S&A) information regarding its CNS shunt product, Delta, and its SCD (siphon-control device). I request that you require an immediate change in its labeling to reflect warnings of adverse events found in medical studies, that you require an immediate notice of these warnings to physicians and patients, and that you institute some restrictions in its use. These same issues and infractions may also be found in Heyer-Schulte Neuro Care's ASD (anti-siphon device) integral shunt, as there was common management to both, and Heyer-Schulte produced the predicate anti-siphon shunt.

The devices are used in the treatment of hydrocephalus, where several thousand are used in the U.S. each year. **The origin of the S&A disparities can be traced to Heyer-Schulte's faulty predicate test data in 1973. Though the FDA may view that the 1976 Device Act precludes Heyer-Schulte, or even PS Medical, from subsequent FDA action on such a matter, PS Medical's labeling upon examination is far too generic and fails to include this adverse data. It appears the manufacturers tried to suppress the adverse data.** The adverse data of the Delta, SCD and ASD devices is published in a series of medical studies and identifies them to suffer adversely elevated intracranial pressure (ICP) events, causing serious injury and additional surgery. Sleeping on the device can also lead to shunt malfunctions. These findings often show up as false negatives upon routine testing.

I petition the FDA to act pursuant to 21 C.F.R. Section 10.30, due to the manufacturer's failure to provide relevant safety and effectiveness data under Sections 860.7(c)(d) and (e), failure to comply with labeling under Sections 807.92(b)(2) and (d), and failure to meet reporting requirements under Section 803.24(a) and (b). The device fails to meet any exemption from

adequate instructions for prescription devices under 801.109(c) and (d). Section 701(a) of the Federal Food, Drug and Cosmetic Act provides the FDA with additional authority in these matters. I also petition the FDA based on information contained in documents provided in my June 27, 1996 "Notice of Safety and Effectiveness Defects," provided to Dr. Anita Kedas at the Office of Surveillance and Biometrics.

STATEMENT OF GROUNDS

A Summary of the Most Recent Scientific Evidence Includes:

1. A 1996 bench and animal study[1] of adverse effects of vertical position and external pressure on Delta valves showed the devices experienced a marked increase in upright opening pressure when implanted at or above the foramen of Monro. They found similar abnormal findings when the device was surrounded by tight overlying scalp, and similarly, from external pressure of a pillow. They reported these findings to cause unhealthful increased intracranial pressure (ICP), resulting in functional obstructions, and further surgeries.

2. An updated 1995 study[2] of shunts, including Delta valves and siphon control devices on a series of live patients and bench tests using the "Heidelberg Valve Test Inventory," found evidence of adverse function from external pressure. The typical patient subcutaneous pressure over the shunt was 3-5 mmHg; with the head touching a soft feather pillow it was 15-20 mmHg; and with the head lying on a hard board it was up to 125 mmHg. They observed dramatic increases in resistance of the Delta, SCD, and ASD shunts from these pressures, with an equal decrease in CSF flow.

3. A 1994 scientific study[3] by PS Medical discusses problems associated with their Delta valves and siphon control devices (SCDs). It states that these shunts placed at the level of the foramen of Monro will experience an increase in shunt opening pressure in the upright position. They suggest placement below the foramen of Monro, noting for each 2 cm of distance below this "zero" point, a decrease of 2 cm H2O in upright opening pressure will occur. They state claims about the Delta that are refuted by scientific data.

4. A 1994 published study[4] of Delta, SCD and ASD shunts found that diffuse external pressure of 5 mmHg over the device caused a drastic decrease in flow in an upright system.

5. A 1991 letter to the editor[5] by Dr. Harold D. Portnoy, co-inventor of the ASD anti-siphon device, states that the SCD device operates from a normally closed position, and thus has no safety factor for preventing abnormally increased ICP. He suggests that the SCD is more likely to fail than his ASD device.

6. A 1991 study[6] examined a series of 50 patients who had been implanted with ASD (anti-siphon device) shunts, predicate to the Delta shunt. They noted a marked increase in ICP in the upright position when the devices were placed at the level of the foramen of Monro, its designed and recommended site, and referred to as the "zero point" for surgical purposes.

7. A 1991 prospective study[7] by Toronto's Hospital for Sick Children of 38 children implanted with ASDs (anti-siphon devices) found 10 patients to experience functional obstruction of the shunt system, with documented patency on shunt flow testing. Three case reports were provided. The authors report that although the SCD device (integral component of the Delta shunt) was not tested, it would present problems comparable to the ASDs.

8. A 1990 study[8] by the University of Oklahoma Health Sciences Center funded in part by Pudenz-Schulte in preparation for Food and Drug Administration approval of its Delta shunt valve, ran a series of bench tests on SCDs, ASDs and standard differential pressure valves. The study focused on the substantial equivalency between the ASD and SCD valve, and did not evaluate the published adverse events.

9. A 1986 study[9] of patients implanted with the predicate anti-siphon device (ASD) found that patients were experiencing ventricular enlargement, increased ICP complaints, and an elevated opening pressure associated with the upright position, often presenting itself as a false negative on routine testing. The author thought that the initial ASD test data was flawed in terms of its upright opening pressure, catheter length, and design.

10. A 1986 letter to the editor[10] from Dr. Harold Portnoy, co-inventor of the ASD, stated in response to criticisms stated that in over 200 surgeries he had not witnessed any such problems with patency and upright ICP.

11. **The 1973 study[11] by Fox, Portnoy and Schulte, inventors of the ASD, the first anti-siphon device, employed unusual test methods in reaching favorable conclusions for the device. In retrospect, the results appear to be flawed. All subsequent devices are based on this original, or predicate, test data.**

12. The Delta's warnings and labeling[12] in its 1990 FDA 510(k) application fails to warn of "measurable" adverse effects on upright opening pressure and ICP from external pressure to the device, or from variations in vertical positioning.

CNS (central nervous system) shunts are used in the surgical treatment of hydrocephalus to drain off excessive amounts of CSF fluid, normally produced, but which an injured brain cannot clear and re-absorb. The shunts reroute the fluid to the heart or

abdomen via a long catheter, which is usually permanent. The anti-siphon shunts are used to reduce "excessive drainage" of CSF fluid in the erect posture, but commonly cause insufficient drainage, increased ICP, and surgical revision. The mounting adverse findings raise serious questions about their routine use.

Medical studies consistently show an association between increased ICP complaints, false negative findings, and a higher incidence of corrective surgeries associated with the use of these shunts. The risks of injury associated with increased ICP are well documented. PS Medical makes an unusual claim that their Delta shunt will not adversely effect the user's ICP.

The failure to warn doctors and patients of the potential serious adverse effects and false negative findings when safer alternatives and labeling information is available, contributes to many hundreds of preventable injuries annually, including irreversible brain damage and possibly death.

The use of Delta, SCD and ASD shunts for the surgical treatment of hydrocephalus must be viewed in consideration of the following information:

1. CNS (central nervous system) shunts are used in the surgical treatment of hydrocephalus as a means to drain off excessive amounts of CSF fluid for the life of the patient. They are intended to maintain the individual patient's intraventricular (CSF fluid) pressure at some sustainable and healthful level.

2. While no single type shunt will work in all surgical treatments, manufacturers are required to provide thorough warnings and use precautions, and to maintain appropriate problem files on their devices. Surgical revisions to place a more appropriate pressure model occur in about one-third of initial shunt placements. The shunts may also become obstructed. Current success rates with shunting range between 50% and 80%, depending more on age and etiology, but also on other factors. These rates have afforded many individuals to lead otherwise normal lives.

3. It is essential that user surgeons be accurately informed of all risks, warnings, and implant precautions via each product's labeling. A generic shunt labeling statement will not suffice.

4. The Delta, SCD and ASD shunts are used in cases of suspected excessive or overdrainage of CSF to reduce outflow in the upright posture, by incorporating a sensor that relies on external (atmospheric) pressure as a baseline for CSF flow. They meet FDA guidelines via substantial equivalency to the ASD device.

5. These anti-siphon shunts have been reported in some cases to reduce the complications associated with CSF overdrainage, but are reported and confirmed to cause insufficient flow in the upright position, and subsequent serious injury.

6. The best available scientific evidence links these shunts to adverse events including: ventricular enlargement, cerebral deficits, headaches, elevated ICP complications, intermittent and possibly permanent obstruction of the shunt system, and disability. These complications are often presented as false negative findings on routine testing, and result in higher medical costs and unnecessary shunt surgeries.

7. The adverse events are due to surgical mal-positioning, and external pressure to the device. In mal-positioning, adverse upright opening pressures and increased ICP occur due to a device positioned at or above the level of the foramen of Monro in a VP shunt system that incorporates a long drainage tube. Similarly, adversely elevated opening pressure and ICP can occur from external (scalp) pressure over the anti-siphon device, which in some cases renders the device unsafe for its intended use. In the Delta, for example, the internal SCD normally reduces CSF flow in the upright posture, but it can close off CSF flow abnormally and remain so, causing adversely elevated ICP via these factors. In all anti-siphon shunts, external pressures during sleep can adversely raise opening pressures and cause intermittent malfunctions, depending on body weight and sleeping surface.

8. In cases where a ventricular catheter is in place at a high up or very low location on the head, the design and implantation techniques of the integral ASD and Delta shunts do not permit an effective placement so as to offset the variation in upright opening pressure. Neurosurgery practice recommends placing shunts immediately adjacent to the exiting ventricular catheter, as it helps to stabilize the position of the catheter.

9. Although the various anti-siphon shunts are different, they all share the same common problems and are based on flawed predicate (ASD) test data, design and labeling.

10. PS Medical's 1990 510(k) Delta labeling fails to alert the user surgeon to adverse information regarding site mal-positioning and follow-up testing. It also fails to provide warnings to patients in regards to potential adverse events during sleep. Heyer-Schulte's ASD labeling has not been examined, but is suspected to be identical.

11. In summary, the present design and labeling of anti-siphon devices does not provide the surgeon and patient with sufficient information to render it safe and effective for routine use. Alternatives to these shunts include the Cordis Orbis Sigma valve, Holter valve, slit valve, and other procedures. There are presently no specific pillows or head covering known to remedy the adverse events of external pressure during sleep.

EVIDENCE OF INCREASED RISKS IN THE USE OF DELTA + ASD SHUNTS

The problems associated with the use of anti-siphon devices

was suspected by McCullough as early as 1983.[9] The most recent study identified safety and effectiveness problems in Delta shunts, Higasha et. al. study[1] published in the Journal of Neurosurgery, Vol. 84, 1996. The study evaluated pressure and flow characteristics of three (3) pressure models of Delta valves in well-designed bench tests, and in animal studies, using the PL1, PL1.5 and PL2 valves, coinciding with low, medium and high pressure. They subjected the Delta valves to bench testing under three types of conditions: 1) Subcutaneous pressure on the valve; 2) Valve implantation site (relative to the foramen of Monro); and 3) Postural hydrostatic differential-pressure changes.

In subcutaneous pressure testing in rats, they noted a steady rise in subcutaneous pressure from the 1st through 6th postoperative day, with the tendency to stabilize thereafter. In bench tests of submerged valves at various depths in water to simulate external pressure, they found a decrease in flow rates corresponding to rising external pressures, testing 0 cm H2O through 12 cm H2O in each body posture. They found the decrease in flow rate and increase in ICP most significant in the erect posture, with a linear correlation between external pressure and closing pressure. They concluded that insufficient drainage and nonphysiological ICP due to subcutaneous pressure is a very real problem in the erect posture.

In evaluating the effects of valve implantation site and head elevation on opening pressure, they found the anti-siphon function of the Delta valve to be significantly affected by the valve position in the shunt system. In the supine position, they found the closing pressure to be within device specifications and physiological ICP range when placed at the level of the mastoid process or the foramen of Monro. But in the erect position, they found the closing pressure was considerably higher when the valves were placed at the level of the foramen of Monro. They concluded that a patient with the Delta valve implanted at this site will have a non-physiologically high ICP in the upright position. This excessive reduction of flow, or functional obstruction, occurs as the patient assumes the erect posture.

The authors state that the tendency to develop shunt adequacy or insufficiency using valves with siphon-reducing devices is determined by the closing pressure of the valve, and the intraventricular pressure (ICP) is gradually adjusted at the approximate closing pressure of the valve after implantation. They conclude that the problem of malfunction of Delta valves and SCDs applies to all patients who have been implanted with them.

A study[2] by Kremer et. al. published in Childs Nervous System, Vol. 11, 1995, evaluated a series of currently available shunt valves, including the Delta Level 1 and 2 valves, applying a set of 16 bench tests to simulate conditions encountered by shunts in the human body. They also recorded subcutaneous pressure in 8 patients using transducers. They found the human subcutaneous pressure was usually 3-5 mmHg. But when the head was

touching a soft feather pillow (head angle 45 degrees), the pressure increased to 15-20 mmHg. When lying on a hard board, pressures of 125 mmHg occurred. Swollen tissues or scars produced values of 10-25 mmHg.

When simulating these conditions under bench testing, they observed dramatic resistance increases with all ASD and the similar Delta (SCD): with 10 mmHg external water pressure they found a resistance increase from 0-1 to 10-11 mmHg, with 20 mmHg external pressure resistance increased to 21-24 mmHg, with 30mm Hg pressure to 28-35 mmHg and so on. The corresponding flow rates tends to zero with a pressure of 5 mmHg.

The authors conclude that anti-siphon devices pose a potential mechanical liability of the shunt system with risks particularly associated with nocturnal shunt obstruction when the patient is lying on the anti-siphon mechanism.

An earlier study[4] by Kremer et. al. Childs Nervous System, Vol. 10, 1994, conducted bench testing on a series of anti-siphon devices, including the Delta Level 1, Level 2, SCD and ASD valves. They incorporated a horizontal and hanging drainage system to simulate different postural positions, with external water pressure to simulate subcutaneous pressure. They found that all of the devices experienced decreases in flow from small amounts of external pressure. **They stated their results underline the need for implantation under a free-floating scalp, however, they question if that is possible in every case.**

A 1994 publication[3] published in Childs Nervous System, Vol. 10, 1994, is authored by PS Medical's David Watson, and discusses the past and present problems with Delta valves, SCDs and ASDs, with some unusual claims. He states:

"Because the resistance to flow reduction is proportional to distal catheter length, location for placement of siphon controlling devices has to be calculated as dependant upon the length of the distal catheter. For example, an adult patient with a 50 cm distal catheter would require device placement approximately 8-10 cm below the foramen of Monro to achieve nullification of the additional 10 cm of back-pressure. Placement of these devices far down on the neck is contraindicated, so only a portion of the increase in back-pressure can be achieved with placement under the loose skin of the scalp."

"The differential pressure across the Delta Valve's inlet and outlet is proportional to the negative pressure acting on the distal catheter..... The net resistance of the shunt system to flow is thereby maintained at a near constant level at any flow rate regardless of patient posture or distal catheter length. **The Delta valve eliminates the need to consider pressure variations due to distal catheter lengths, because its resistance to flow is proportional to all negative distal hydrostatic pressures. However, the Delta valve, like all valves, cannot discriminate**

between inlet hydrostatic pressures and inlet intracranial pressures. For this reason, minor adjustments to the total resistance of the shunt system can be made by positioning the Delta valve higher or lower on the shunt system."

"For example, positioning the Delta valve on the skull 2 cm lower than the foramen of Monro will result in an upright decrease in shunt back-pressure, and consequently ICP, by 2 cm of water." Watson then contradicts this cause and effect of shunt opening pressure on ICP by stating, "ICP is not adversely influenced by the Delta shunt. The patient's own physiologic mechanism will regulate normal pressure-induced ICP variations."

It is postulated that a 10 cm higher position would result in an increase of 10 cm of upright opening pressure. However, a 10 cm change in shunt upright opening pressure is reported as significant by both Higashi and Chiba.

It appears that the 1991 study and paper[6] by Chiba, et. al., Neurosurgery, Vol. 29, No. 4, 1991, caused years of debate and speculation to end, with the two manufacturers agreeing to a change in implantation methods. Chiba studied a series of 50 adult patients, ages 16-70 years, 33 men and 17 women, implanted with shunts incorporating ASDs at different sites in the head and neck, and drafted elaborate mathematical formulas to determine the most functional placement site. He concluded that with placement at the level of the foramen of Monro, "The least ICP required to open both the shunt valve and the ASD must be greater than 12 cm H2O. Because this is much higher than the average ICP in erect adults, it is difficult to initiate shunt flow."

Chiba's published work resulted in a comment to the editor[5] by Dr. Harold Portnoy, co-inventor of the anti-siphon device, Neurosurgery, Vol. 29, No. 4, 1991. He writes:

"The ASD has a built in safety factor. The device is normally open and requires at least 10 cm H2O negative pressure to activate closure of the device. This safety factor was built into the ASD because we were concerned that the overlying scalp could exert a pressure on the diaphragm of the device, which would act as if there was excessive negative pressure within the valve. The present (Chiba) paper would seem to support the wisdom of including the safety factor but suggests that the safety factor may be inadequate. The siphon control device (SCD) is identical in function to the ASD, except that the SCD is normally closed and thus has no safety factor. This paper would suggest that the SCD is even more likely to fail than the ASD."

"Placing the ASD 10 cm distal to the DPV usually places the ASD in the subcutaneous tissue of the neck, a place for which the device was not designed. Although our Japanese colleagues have not had any problem with subcutaneous placement of the ASD, others have with resulting malfunction of the shunt."

A 1991 study[7] at Toronto's Hospital for Sick Children, published in Pediatric Neurosurgery, Vol. 17, 1991-1992, evaluated case histories of 38 children implanted with ASD shunts. They found 10 patients to experience functional obstructions of the shunt system, with documented patency on shunt flow testing. They concluded that external pressure, which is in fact tissue pressure over the device, can be considerably greater than atmospheric pressure, and that these external pressures will increase the resistance of the ASD, decreasing CSF flow. The authors report that although the SCD device (integral component of the Delta shunt) was not tested, they believe it would present problems comparable to the ASDs.

The 1990 study[8] by Horton, et. al. at the University of Oklahoma Health Sciences Center, published in the Journal of Neurosurgery, Vol. 72, June 1990, conducted bench testing on the ASD, SCD, and several shunts without any anti-siphon device for comparison. The study was provided to the FDA in 1990 as part of PS Medical's 510(k) application for its Delta valve. They write:

"The PS Medical SCD is 0.94 cm in diameter and its maximum profile height is 0.43 cm. It is a normally closed ASD in which the orientation of the device is not as critical because there are two silicone diaphragms that inhibit flow into the twin outlet ports. There is also an offset ring exterior to both diaphragms in order to prevent the overlying scalp from occluding the apparatus."

"As with the ASD, the SCD is best placed in a loose subgaleal pocket and not in tissues of the neck, chest or abdomen..... Based on laboratory experiments and clinical observations, Foltz (personal communication, 1989) suggested that the SCD be placed in tandem immediately distal to the differential-pressure valve and on the same level as the tip of the ventricular catheter."

"In our clinical experience, the small amount of additional resistance added to a shunting system with low opening pressure by an in-line PS Medical SCD does not adversely affect intra-ventricular fluid drainage, as measured by isotope clearance from the reservoir of the differential-pressure valve. Only time and experience will allow comparison of the favorable in vitro flow performance of the SCD in association with presently available shunt valves to its function in a clinical setting."

A 1986 paper[9] by McCullough, et. al., published in Neurosurgery Vol. 19, No. 4, 1986, evaluated 40 children and young adults implanted with ASDs. He found that 9 patients encountered adverse complaints, in spite of testing that showed patent shunts. In 4 of these, there were alarming neurological problems of coma or severe headaches. Shunt patency was documented in the horizontal position, but CT scanning revealed progressive ventriculomegaly when erect. Complaints abated and ventricular size diminished after converting to a standard valve.

McCullough wrote: "Although there is no absolute proof that ASD mal-positioning produced these complications, the circumstantial evidence is compelling. Multiple shunt taps, flow studies, and surgical explorations verified shunt patency and normal intracranial pressure (ICP). The symptomatic improvement and the decrease in ventricular size after placing patients in horizontal positions supports the theory that the basic problem involves opening pressure in the upright position. The patients all had ASD units with VP systems, and they were all relatively tall children or adults."

A 1986 letter to the editor[10] published in Neurosurgery Vol. 19, No. 4, 1986, is a response by Dr. Harold Portnoy, co-inventor of the ASD device, to critical reports of the device by McCullough. Dr. Portnoy writes:

"With keen observation, McCullough noted that the symptoms were related to erect posture. In my experience of implanting over 200 shunts with ASDs, I have not witnessed a patient in whom symptoms were produced on attaining the erect position and the shunt was found to be patent on testing."

The original anti-siphon test study[11] by Fox, Portnoy and Schulte, published in Surgical Neurology, Vol. 1, Sept. 1973, performed a series of in-vitro bench tests of the ASD valve and revealed concerns of the adverse events now well described. The authors viewed this as not significant. But in retrospective examination, there are peculiarities in the test methods that measured closing and opening pressures. Additionally, it is unclear whether they utilized a 80 cm distal catheter, or 60 cm catheter length, as the longer the distal catheter, the higher the upright opening pressure will be. This point was also raised by McCullough in 1983. The authors wrote:

"Changing the position of the anti-siphon valve (i.e., either moving it above the proximal reservoir or closer to the lower distal reservoir) did not alter the flow rate once flow was initiated. However, the opening and closing pressures were changed. The higher the anti-siphon valve above the 0 mm baseline of the manometer, the greater the closing pressure by an amount in millimeters of water equal to the change in height of the anti-siphon valve. The reverse occurred if the valve was lower (closer to the distal reservoir). The higher the valve, the greater the opening pressure (by about +20 mm of water for each 100 mm increase in height)."

"It can be shown in vitro that whereas the location of other standard valves on shunt tubing (i.e., either close to the ventricle or at the distal end in the upright patient) has no effect per se on the opening or closing pressures, or the flow rate, the location of this anti-siphon valve could be critical in the upright patient.... In actual practice, we have found that placing the anti-siphon valve 50 mm above or below the foramen of Monro seems to have little measurable clinical significance."

"The purpose of the anti-siphon valve per se is to prevent excessive negative intracranial pressures in the upright patient. Of course, the addition of internal and external resistances in the system will have the effect of raising both the opening and closing pressures as well as reducing the flow rate."

In regards to PS Medical's labeling, their 1990[12] FDA 510(k) Delta labeling and package labeling up to 1994 does not include any of the adverse information described herein either under "Warnings," "Contraindications," "Precautions," or "Complications." Rather, the information appears to be taken verbatim from a neurosurgery textbook of standard shunt labeling. Under "Instructions for Use," there is a brief mention to place the shunt under a surgically created sub-galeal pocket. It reads:

"A variety of surgical techniques may be used in placing the Delta CSF-Flow Control Valve on the skull. The site of placement is at the discretion of the surgeon."

"It is suggested that the Delta CSF-Flow Control Valve be placed in a surgically created subgaleal pocket and not under the scalp incision. The Delta CSF-Flow Control Valve should not be placed under the skin of the neck, chest or abdomen."

The above studies published since 1991 meet all of the accepted scientific criteria for supporting a causal link between the various anti-siphon shunts, and harm. (1) The evidence shows a direct correlation with the use of these shunts, and an increased risk of specific adverse events; (2) This association is consistent throughout the studies, with some admissions in a paper by PS Medical; (3) The risks increase with increasing use and period of implantation; and (4) There are documented biological and physiological explanations of how these shunts cause their adverse events; (5) The adverse events originated from the faulty design and test data of the predicate anti-siphon (ASD) shunt. The evidence is equally causal with the Delta, SCD device, and ASD device shunts.

The more alarming aspect of this device problem is that it can present itself as a false negative finding, and that an array of new test procedures is needed if these devices are to be continued in use. In human studies, the adverse effects were seen more in taller children and adults. But, there is no conclusive data to exclude young children and infants from adverse events associated with external scalp pressure or pressure during sleep. It is felt that restrictions, in addition to specific warnings, need to be placed on the use of these devices.

ACTIONS REQUESTED

This Citizens Petition invokes the FDA to take action under 21 C.F.R. Sections 10.30, 10.33, and 10.35. The FDA has a duty to investigate manufacturers for FDA infractions, including criminal

prosecution, and to examine new reports of adverse events associated with Class II medical devices. Section 701(a) of the Federal Food, Drug and Cosmetic Act also provides the FDA with additional authority in these matters.

This Petition alleges that Pudenz-Schulte, and possibly Heyer-Schulte, failed to meet FDA and GMP regulations in the manufacture and distribution of the ASD, SCD, and Delta devices, and may have conspired to suppress reported problems. It appears based on FDA records that Pudenz-Schulte failed to notify them of field reports citing specific adverse findings with their Delta and SCD shunts. Their Delta 510(k) application makes no mention of the adverse SCD reports. Yet, they appear to have made later structural changes to the design of the Delta, short of giving notice to the FDA.

Examination of PS Medical's MDR (Medical Device Reporting) reports filed with the FDA reveal numerous reports of surgical revision due to "improper flow or pressure characteristics." But without these new warnings and precautions, it is difficult for a surgeon to understand the cause(s) of the shunt malfunctions, as well as preparing full and complete MDR reports.

The Following FDA Code Sections are Applicable:

1) Fails to identify necessary safety and effectiveness data under Sections 860.7(c)(d) and (e).
2) Fails to meet device labeling standards under Sections 807.92(b)(2) and (d).
3) Fails to meet reporting requirements under Section 803.24(a) and (b).
4) Fails to meet instructions exemptions for prescription devices under 801.109(c) and (d).

This Petition Requests the Following Immediate Actions:

1. Require the manufacturer to amend its FDA 510(k) labeling to include the following warnings, precautions and use instructions regarding:

   a) Adverse affects on shunt opening pressure, and ICP, from implantation sites relative to the foramen of Monro, with test methods to calculate effect on opening pressure.

   b) Adverse affects on shunt opening pressure, and ICP, from external overlying scalp pressure, with test methods to calculate effect on opening pressure.

   c) Adverse affects on shunt opening pressure, ICP, and possible shunt malfunction from external pressure caused by inadvertent sleeping on the device.

2. Require a new package insert to warn of adverse events (a), (b), and (c) above.

3. Require the manufacturer to conduct immediate testing of its subject shunt for adverse events under conditions of normal sleep and external pressure, and make those findings available to physicians and patients.

4. Require that the surgical installation and precautions section of the manufacturer's product packaging implicitly describe the information in (a), (b), and (c) above.

5. Immediately inform all U.S. neurosurgeons and neurologists through a "Dear Doctor Letter" about the new warnings and labeling changes, and encountered false negative findings.

6. Immediately inform all other U.S. professionals through the FDA Medical Bulletin about the new warning and labeling changes.

7. Impose restrictions in the use of these devices.

CONCLUSION

This petition to require new warnings on Delta, SCD, and the similar ASD shunt, concerns the safety of an estimated several thousand Americans per year who will be implanted with them. It has been demonstrated that these devices cause specific adverse events and injury not described in their present labeling and packaging, and that these adverse events were noted and dismissed in 1973 predicate test studies. As the present labeling does not identify this adverse information, this Petition requests that immediate warnings go out to surgeons and patients, that the manufacturers amend their product labeling, and that the FDA impose restrictions on its use. No FDA policy or exemption should preclude device manufacturers from meeting such labeling and reporting standards necessary for the safe use of their product.

I wrote directly to PS Medical and to UCLA Medical Center, a known active user of these shunts. Both declined to respond, including UCLA's failure to comply with a request pursuant to the California Public Records Act.

I urge the FDA to exercise its public health responsibility by warning the nation's health care professionals and patient users of the specific risks and complications associated with these shunt devices. I also urge the FDA to exercise its duty in investigating the manufacturers for FDA infractions and/or criminal violations. Thousands of Americans will be implanted with these shunts each year and will not be provided with the necessary warnings in which to avoid potential serious injury, as well as make an informed decision regarding their care.

ENVIRONMENTAL IMPACT STATEMENT

The petitioner hereby states that the relief requested in this petition will have no environmental impact and that, therefore, an environmental assessment is not required.

CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are adverse to the petition.

Dated: 11/6/96 By: Stephen M. Dolle

Stephen M. Dolle
Hydrocephalus Researcher
13191 Gwyneth Drive #A
Tustin, CA 92780
(714) 669-9991

REFERENCES

1. Journal of Neurosurgery, Vol. 84, 1996: Mahmood Hassan, M.B., B.S., Sotaro Higashi, M.D., Junkoh Yamashita, M.D.; "Risks in Using Siphon-Reducing Devices in Adult Patients with Normal-Pressure Hydrocephalus: Bench Test Investigations with Delta Valves."

2. Childs Nervous System, Vol. 11, 1995; Updated version of an oral presentation from the Consensus Conference Hydrocephalus, Italy 1992: A. Aschoff, P. Kremer, C. Benesch, K. Fruh, A. Klank, S. Kunze; "Overdrainage and Shunt Technology: A critical comparison of programmable, hydrostatic and variable-resistance valves and flow-reducing devices."

3. Childs Nervous System, Vol. 10, 1994; Presented at the Consensus Conference Hydrocephalus, Italy 1992: David A. Watson, Product Development, PS Medical; "The Delta Valve: a physiologic shunt system."

4. Childs Nervous System, Vol. 10, 1994; Presented at the Consensus Conference Hydrocephalus, Italy 1992: P. Kremer, A. Aschoff, S. Kinze; "Risks of Using Siphon-Reducing Devices."

5. Neurosurgery, Vol. 29, No. 4, 1991: Harold D. Portnoy, M.D.; "Comment (to Dr. Chiba's paper)."

6. Neurosurgery, Vol. 29, No. 4, 1991: Kazuhiko Tokoro, M.D., Yasuhiro Chiba, M.D.; "Optimum Position for an Antisiphon Device in a Cerebrospinal Fluid Shunt System."

7. Pediatric Neurosurgery, Vol. 17, 1991-1992: Marcia C. da Silva, M.D., James M. Drake, M.D.; "Complications of Cerebrospinal Fluid Shunt Antisiphon Devices."

8. Journal of Neurosurgery, Vol. 72, June 1990; Study funded by Pudenz-Schulte and Included in 1990 Delta 510(k) Application: Donald Horton, M.D., Michael Pollay, M.D., University of Oklahoma Health Sciences Center; "Fluid Flow Performance of a New Siphon-Control Device for Ventricular Shunts." (1989 PS Medical-Funded Study)

9. Neurosurgery Vol. 19, No. 4, 1986: David C. McCullough, M.D.; "Symptomatic Progressive Ventriculomegaly in Hydrocephalics with Patent Shunts and Antisiphon Devices."

10. Neurosurgery Vol. 19, No. 4, 1986: Harold D. Portnoy, M.D.; "Letter to the Editor (Comment to Dr. McCullough's 1986 criticism)."

11. Surgical Neurology, Vol. 1, Sept. 1973: John L. Fox, M.D., Harold D. Portnoy, M.D., and Rudolph R. Schulte; "Cerebrospinal Fluid Shunts: An Experimental Evaluation of Flow Rates and Pressure Values in the Anti-Siphon Valve."

12. Pudenz-Schulte Medical Research Corporation's labeling from its 1990 510(k) FDA Application for Delta shunt.