HIGH-PRECISION COMPOUNDING AND CONTROLLED DOSING SYSTEM FOR OCCUPATIONAL HAZARDOUS DRUGS

By

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ABSTRACT

Effect of hazardous drugs on pharmacists, compounding issues and distribution errors are three major risks that are still associated with the medication processes. Risks associated with handling the hazardous drugs have been addressed since 1970's. Due to non-selective mode, antineoplastic agents have many adverse effects on the health of patient as well as the health of healthcare workers. Many studies showed that people working in such contaminating workplaces have traces of antineoplastic agents in their body even if they are not handling antineoplastic drugs directly. Hazardous outcome of oncology drugs can be minimized by developing an automated closed transfer system. Beside hazardous effects of drugs, main medication issues are compounding errors and distribution errors. A literature review has been conducted to analyze four themes of drug compounding which if ignored can lead to serious medication errors. Possibilities of distribution errors have also been discussed. After a detail analysis, possible solutions for all these issues have been presented. Design methodology of thesis has been developed to make a high-precision compoundind and controlled dosing system for occupational hazardous drugs. Software routine of presented system acts as a quality plan for compounding process which keeps the pharmacists and nurses adhered to a specific protocol. Features like high-accuracy, barcode medical administration (BCMA), electronic medication records (eMARs), customized label printing and automatized calculation routine inhibit occurring of many compounding and distribution errors.

Keywords: Hazardous drugs, compounding errors, distribution errors, high-precision automated drug preparation.

ÖZET

İlaçla tedavi süreçleriyle ilgilendirilen 3 önemli risk; tehlikeli ilaçların hastane eczacıları üzerindeki etkisi, elle ilaç hazırlama sorunları ve dozlama hatalarıdır. Tehlikeli ilaçlara dokunma sorunu 1970'den beri pek çok kez incelenmiştir. Seçici olmayan modları sebebiyle, antineoplastik ajanların hem hastanın hem de sağlık çalışanlarının sağlığı üzerinde birçok olumsuz etkisi vardır. Çoğu araştırma kontamine yerlerde çalışan insanların vücudunda, ilaçlara dokunmasalar bile, antineoplastik ajanların izine rastlandığını bildirmiştir. Onkoloji ilaçlarının tehlikeli sonuçları, otomatik olarak çalışan kapalı bir transfer sistemi geliştirerek en aza indirgenebilir. İlaçların zararlı etkilerinin yanı sıra, bileşik hazırlama ve dağıtım hataları diğer temel ilaç tedavisi problemlerindendir. İlaç bileşimi hazırlamanın 4 maddesini analiz etmek için bir literatür taraması yürütülmüştür. Zira bunlardan birini yok saymak ciddi ilaç tedavisi hatalarına neden olabilir. Dozaj hatalarının sebepleri de araştırılmış ve detaylı bir analizden sonra, muhtemel çözümler sunulmuştur. Tezin tasarım yöntembilimi; yüksek hassasiyetli ilaç hazırlayan kullanıcı kontrollü bir dozlama sistemi geliştirmektir. Sistemin yazılım rutini bileşik hazırlama işlemi için bir kalite planı olarak davranmaktadır. Bu da hastane eczacıları ve hemşireleri belirli bir protokole bağlar. Yüksek hassasiyet, medikal barkod sorgulama, elektronik medikasyon kayıtları, özelleştirilmiş etiket basımı ve otomatik hesaplama rutini gibi özellikle birçok ilaç hazırlama ve dozlama hatasının oluşumunu önler.

Anahtar kelimeler: Tehlikeli ilaçlar, elle ilaç hazırlama hataları, dozlama hataları, yüksek hassasiyetli otomatik ilaç hazırlama.

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1 INTRODUCTION

In 1984 the institute of medicine estimated that 98,000 patients die each year in US due medical errors. In 1999 same institute publish a report which brought the issue of medical error in the front line [1]. Since last two decades this figure has been raised to 210,000 deaths per year [2]. These errors include errors in compounding system like accuracy problem, medicine identification error and wrong label description. Inferior quality of medicine may also cause serious errors. Medical errors also involve errors in giving wrong medicine to wrong patient and other dosing errors. Many publications emphasis on the need of implementation of any improved design of healthcare procedure. The institute of medicine published a report on "Crossing the Quality Chasm" [3], emphasizing on six aims for improvement of health care routine. Beside medication error another big problem in hospitals and pharmacies are the possible hazardous effects of the drugs on health of medical staff. The pharmacists, nurses and others staff involved in the preparation, handling and infusion have the highest potential exposure to these antineoplastic agent [4]. In today's market, few engineering solutions exist but they do not provide solution to compounding issues, distribution issues and possible occupational hazardous effects all together in one compact design.

1.1 Problem Statement

Effect of hazardous drugs on pharmacists, compounding issues and distribution errors are three major risks that are still associated with medication processes. Intensive study has been done to improve compounding and distribution system for more than five decades. Patient safety is a global issue which requires knowledge of both human factors involved and the system engineering. In this thesis, needs of technology are first recognized to eliminate medication errors and hazardous effects, then by going through a detailed analysis, a system has been designed featuring a high-precision compounding and error free, controlled dosing system.

1.2 Dissertation Outline

In this study the problem statement is deeply addressed by reviewing literature of the effects of hazardous drugs used in chemotherapy and medical error issues. Later in this thesis detail

methodology has been presented along with description of design development. Below is the detail of each chapter of this thesis.

Chapter 2 provides the literature review of three fundamental issues related to drug dosage system. Chapter addresses significance of each issue and discusses present technologies for each of them. First issue is related to the hazardous effects of harmful drugs on the healthcare providers. Second problem is compounding issue and lastly proposed solutions of distribution errors in literature have been discussed.

Chapter 3 proposed the solution of the problem statement. Analyzing the problems in literature review, feasible solutions have been proposed. According to these solutions methodology of the system has been described in detail. System's hardware and graphical interface modelling has been done in this chapter.

Chapter 4 describes the hardware detail and accuracy analysis of this project. Wiring, connection interfaces and settings of all hardware devices have been shown in detail. After developing hardware, accuracy analysis of the hardware has been done.

Chapter 5 all phases of software development have been described. It gives details of interfaces technique and data transfer between low-level control, mid-level control and supervisory control. This chapter also provides flow chart and details of controlled software routine.

Chapter 6 provides explanation of hardware and software interfacing of three interfaced devices. Interface devices include camera, barcode scanner and printer. Hardware connectivity method of each has been described in detail. Then, software graphical user interfaces for each and coding principal behind each has been discussed.

Chapter 7 user guide has been provided for quick assistance to use the system. This guide is attended to provide help to pharmacists and nurses.

Chapter 8 provides troubleshooting details of hardware and software. Chapter has been integrated in to main section, one describes troubleshooting that can be done by user during the system, second describe troubleshooting routines that can be followed by the technician.

2 GENERAL REVIEW OF DOSAGE COMPOUNDING AND DISTRIBUTION SYSTEM

The measured rate of medication errors, contamination during compounding and impact of hazardous drugs on medical staff imply that in spite of all control processes resultant ratios are a long-standing threat to medical safety. Therefore, developments are still needed to improve medical safety.

The objectives of this chapter are to (1) describe possibility of hazardous effects of drugs on pharmacists, (2) briefly discuss compounding issues, (3) summarize types of distribution errors and their clinical and economical significance, (4) review and critique existing techniques and new developments in dosage systems.

2.1 Significance of Hazardous Drugs

The chemicals used in cancer treatment which inhibit cellular growth and destroy malignant cells are known as antineoplastic agents. However, due to the non-selective mode of antineoplastic agents, normal and healthy cells may also be harmed. These agents have many adverse effects on the health of patient as well as the health of healthcare workers. The very nature of treatment with these agents makes it destructive for cancer cells hence making it significant for cancer patient to fight against the disease. Also there are many side effects on the patients as well as on the healthcare staff. Skin absorption, accidental spills, workplace contamination and air contamination can be routes of exposure to these antineoplastic agents. Furthermore, in many hospitals workers do not change their gloves after a recommended time that is why drug samples have been found on the internal side of gloves [4]. The presence of antineoplastic agents and cytostatic drugs on the skin and in the body can cause certain acute and chronic problems as well as infant malformations during pregnancy and even the miscarriage. Acute effects or short term effects may involve skin rash, hair loss or certain allergies. Chronic effects or long-term effects that may be seen are infertility, liver disinfection, formation of leukemia and cancer development in healthcare workers handling antineoplastic agents [5].

Risks associated with handling hazardous drugs have been addressed since the 1970's. After Falck studied urinary mutagenicity [6], many studies showed that people working in such contaminating workplaces have traces of antineoplastic agents in their urine even if they are not handling drugs directly, as shown in Table 2-1.

Table 2-1 Urinary levels of CP, IF, Pt and MTX in personnel present at preparation and administration of antineoplastic drugs [4]

Antineoplastic Drug	No. of positive samples (%)	Range (ng/l)
Cyclophosphamide	18/62 (29%)	50–10 030
Ifosfamide	1/62 (1.6%)	150
Platinum	3/62 (4.8%)	920-1300
Methotrexate	0/62 (0%)	

The table shows results of Roberta Turcu's study [3]. It summarizes biological monitoring of 17 subjects for two consecutive days sampling. Biological supervision of these samples proved this analytically that measurable traces of CP, IF and Pt are present in the urine of both drug preparing and drug administering staff. Additionally, environmental results show that exposure to hazardous drugs is mainly because of incorrect handling procedures [4]. Table 2-1 confirms that uptake of hazardous drugs also depends upon dosage amount of drug. As shown in table 2-1 MTX has zero samples.

2.1.1 Technologies to Reduce Hazardous Effects of Drugs on Healthcare providers

2.1.1.1 Closed Drug Transfer System

Outcomes of hazardous drugs can be minimizing by taking following steps;

- Special attention should be given to the safety of hoods.
- Exposure route of cytostatic drugs is most likely dermal uptake.
- Automation of drug compounding/transfer system can minimize the risk of hazardous effects of cytostatic drugs.

The effects of hazardous drugs addressed the need of closed-system drug transfer devices (CSTD's). In response to all scientific studies on hazardous effects of cytostatic drugs, the American National Institute for Occupational Safety and Health (NIOSH) released an alert warning that a closed system drug transfer device should be used whenever any hazardous drug has to be prepared. The NIOSH defines the closed-system drug transfer devices as: "device is a drug transfer device that mechanically prohibits the transfer of environmental

contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system [NIOSH]".

The International Society of Oncology Pharmacy Practitioners, ISOPP, divides the NIOSH definition of the closed system into two categories;

- "The first defines 'closed' in terms of microbiological contamination. This definition deals purely with introducing micro-organisms into a sterile product, and there is no consideration of the sterile product coming out of the vial contaminating the environment" [ISOPP].
- "The second category defines 'closed' in relation to chemical contamination and refers to drug transfer devices that mechanically prohibit the transfer of environment contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system. ISOPP, however, agree that the NIOSH definition is the most comprehensive and complete" [ISOPP].

However currently there are no official specifications for CSTD's available. Therefore, some studies validate each system against the recommendations proposed by ISOPP and the NIOSH. A study selected titanium tetrachloride to observe the escape of vapor from each product. Figures 2-1, 2-2 and 2-3 show the results of vapor the escape from each device [7].

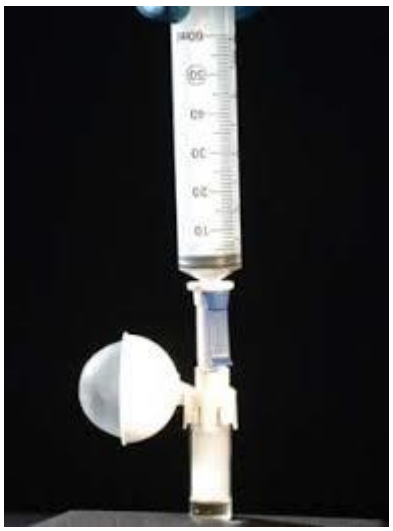

Figure 2-1: PhaSeal with no release of titanium smoke [7].

Figure 2-2: Alaris Smart Site with release of titanium smoke [7].

Figure 2-3: Chemo MiniSpike Plus with release of titanium smoke [7].

This study concluded that only 1 of the 5 devices meet the criteria of CSTD's [7]. That is why, relying and thus handling closed drug transfer devices is not a solution to minimize effects of hazardous effects of drugs.

2.1.2 Automated Drug Dosage Systems:

Advance technology has replaced health care workers and human compounders with robots to reduce exposure to hazardous drugs. Robots and automated drug dosing systems are not only safe and sterile but they are also accurate in compounding. CytoCare from Health Robotics, Apoteca Chemo from Loccioni Humancare, and RIVA (Robotic IV Automation) from Intelligent Hospital Systems present automated solutions to the compounding of hazardous drugs [8]. But recently, a few drawbacks have been reported about robotic drug dosage systems. One of these drawbacks is bacterial contamination in IV drug compounding robots [9]. Therefore, stringent safety measures according to a quality assurance plan should be taken while using a robotic compounding system. In order to clean and load the robot periodically, human assistance is needed and there are sufficient chances of spill and skin contact. Therefore robots are helpful only in making the compounding more accurate, but although they reduce contact with hazardous effects, there are still many chances for hazardous effects on health care workers.

2.2 Drug Compounding Errors

Drug compounding is an important cornerstone in current medication processes. Compounding is a creation of a unique drug specific to an individual, on the prescription of doctors under medical laws. Drug compounding is an essential step in preoperative, intraoperative, and postoperative care. According to the United State Pharmacopeia Convention, a compounding product is;

"The sterile product that includes preparations prepared according to the manufacturer's labeled instructions and other manipulations when preparing sterile products that expose the original contents to potential contamination, as well as preparations that contain non-sterile ingredients or employ non-sterile components and devices that must be sterilized before use" [10].

Since 2012 and 2013, after the outbreak of fungal meningitis due to contaminated compounded steroid injections prepared by the New England Compounding Company (NECC), compounding risks have been highlighted in media headlines [11]. Several studies have brought to light the risks associated with drug compounding. The regulatory authorities

drew the attention of health care professionals to their ethical and professional roles and to adhere to regulatory standards. Contamination of compounded drugs has the highest potential to cause serious infection and threat to a patient's life. Therefore not only should the pharmacists be aware of contamination risks but also nurses and direct care providers should know the guidelines and practices to reduce the risk of contamination during sterile compounding processes.

There are four common themes that lead to successful and productive compounding:

a. **Quality:** Quality includes proper identification, purity, compatibility and stability of the product. Error in product identification can happen due to sound-alike or a look-alike name of the drugs or even if the packaging is similar. Quality in terms of purity means the drug should be free from foreign particles or the environment of the compounding process should be clean and there should be no contamination from foreign particles. Stability means factors like exposure to light and humidity level should not degrade product less than 10%. Compatibility means that the resultant product after combination of two compounded drugs should be known.
b. **Environment:** The technical environment should be sterile. Moreover, preoperative personnel or pharmacists should know all the possible threats to the sterility of the compounded drug. Compounding has been segregated into specialized areas having different level of particulate matter inside the room air. Threats due to microbial contamination and contamination due to air particulate can be reduced by preparing compounded drug into recommended areas by International standards. According to risk of contamination, different compounding drugs should be prepared in different areas. Table 2-2 shows the classification of areas according to ISO.

Table 2-2: Airborne Particulate Cleanliness Class Comparison by Federal and ISO Cleanroom Standards

ISO 14644-1 ISO Class	FEDERAL STANDARD 209E English	Metric
ISO 1		
ISO 2		
ISO 3	1	M1.5
ISO 4	10	M2.5
ISO 5	100	M3.5
ISO 6	1,000	M4.5
ISO 7	10,000	M5.5
ISO 8	100,000	M6.5

Health care providers can reduce environmental contamination by reducing particulate matter in the air and assuring good hand hygiene. Proper cleaning of work places and equipment also helps a lot to improve the environment.

c. Personal Activities: There are some serious threats to the compounding drugs other than the contamination. Most of them are due to wrong mental calculation. This wrong calculation result in wrong concentration of the final product. Another reason for the personal error is due to conversion between metric and non-metric measurement systems. Most of the pharmacies work with metric system but many times conversion is needed, for example weight of the patient from pound should be converted to kilogram.

Another confusion in total vial contents verses product concentration lead to compounding errors. For example preparation of 10mg/ml concentration is actually delivering 100-mL bottle containing 1,000 mg contents. Pharmacists bear responsibility for ensuring the accuracy in all of these risk areas [10]. Additionally, pharmacists are responsible for ensuring accuracy in identification, measurement, mixing and dilution. They also have to be accurate in labelling, storage and distribution of the prepared medicine.

d. Control Process; The last theme that lead to successful and error-free compounding is to define a controlled quality improvement plan. Compounding pharmacies should

collaborate with members of quality and safety department. Whole staff should execute a robust quality improvement process. Such quality improvement plan should include patient monitoring, adverse effect reporting as well as record keeping. Plan should keep pharmacists adhere to a specific routine. For example, first of all pharmacists should identify all products; they have to confirm that they have right product and right concentration. Then they should confirm that product is not expired. Additionally, all the rules of environmental compliance should be known to the compounding pharmacist and nurses. They should ensure workplace is not contaminated, if it is then pharmacist or nurse there self has to clean by applying disinfectant to the surface. Quality plan should also consider the performance of hand hygiene before compounding. Pharmacists should not have any rashes, sunburn or any condition that can cause shedding [10].

2.2.1 Technologies to Reduce Compounding Errors:

2.2.1.1 Bedside Charting Technology (BCMA)

Bedside charting technology or barcode medication administration, also known as electronic charting is another effort to ensure patient safety. It provides dose in a package having barcode label on it. Before administration nurse need to scan the label and cross check the information. In order to use this system effectively, medication delivery system should be standardized and all the pharmacy standards should be structured together [12].

2.2.1.2 Computerized Prescriber Order Entry (CPOE)

Studies proved that system of computerized prescriber order entry for compounding has reduce the medication errors up to 55% [13]. Another research performed by the same group, revealed that CPOE reduce 88% of serious medication errors [14]. Another similar study performed by Vanderbilt University Medical Center showed that 95% of medication errors has been reduce in pediatric critical care [15]. By integrating CPOE system to BCMA, more significant improvements in safety and error free medication [16].

2.2.1.3 Electronic Medication Administration Records (MARs)

Medical administration records, also known as drug charts, are somewhere now computerized. Electronic Medical Administration Records are abbreviated by eMARs. Study on the performance of BCMA with paper MARs concluded that the probability of medication errors is even more high and decreased the productivity of health care staff [17]. In

comparison with paper MARs system, electronic medication administration records are much more significant in reducing medical errors by reducing the human factor.

2.2.1.4 "Smart" Intravenous Devices

Errors during intravenous administration are most common in medication errors [18]. Through simplified programmed software, the smart intravenous devices can considerably reduce the chance of error. These intravenous pumps can reduce the likelihood of tenfold overdose. Thus solving a major problem in pediatrics where most of errors are associated with over dosage.

2.3 Distribution Errors

2.3.1 Definition:

A distribution error is a discrepancy or an error between a prescription and the medicine delivered to the patient or distributes to the ward, it also include the distribution of a medicine with inferior pharmaceutical or informational quality [19, 20].

2.3.2 Categories:

Following are the categories of distribution errors: [21]

- Dispensing medicine for the wrong patient (or for the wrong ward)
- Dispensing the wrong medicine
- Dispensing the wrong drug strength
- Dispensing at the wrong time
- Dispensing the wrong quantity
- Dispensing the wrong dosage form
- Dispensing an expired or almost expired medicine
- Omission (i.e. failure to dispense)
- Dispensing a medicine of inferior quality (pharmaceutical companies)
- Dispensing an incorrectly compounded medicine (compounding in pharmacy)
- Dispensing with the wrong information on the label
- Incorrect patient name
- Incorrect drug name
- Incorrect drug strength
- Incorrect instruction (including incorrect dosage)

- Incorrect drug quantity
- Incorrect dosage form
- Incorrect expiry date
- Omission of additional warning(s)
- Incorrect pharmacy address
- Other labelling errors

2.3.3 Fundamental causes of distribution errors:

Different studies show different causes of distribution errors. A study in UK hospital, researchers took self-reported error cases and used semi-structured interviews of healthcare staff. According to this study [22], there were 106 error-producing conditions were mentioned. The most common causes were: 21% due to busy routine, 12% due to being short-staffed, 11% due to time constraints, 11% because of fatigue of healthcare providers, 9.4% due to interruptions during dispensing, and 8.5% due to look-alike/sound-alike medicines.

Another study based in Denmark showed the fundamental causes of distribution errors were: unreadable handwriting of the prescriber, 'traps' i.e. look-alike and sound-alike medications, absence of effective communication and lack of concentration due to interruptions [23].

2.3.4 Strategies for the Improvement:

Over the decades, pharmacists have introduced many strategies to lower the rate of distribution errors.

2.3.4.1 Barcode System

With barcode system, rate of distribution and dispensing errors in a US hospital reduced from 0.19 to 0.07%. While cost-benefit analysis revealed that the revenue curve met with that of cost during the first quarter of the fourth year [24].

2.3.4.2 Semi-Automated Medication Cabinets

Another approach to reduce drug distribution error is to use semi-automated medication cabinets. This system also uses barcode system and a carousel filling process. Carousel gets filled by a semi-automated system. These stored medicines are .non-refrigerated type. There is another two days filling process, in which cabinets are filled manually and health care staff retrieves medicines from shelves manually. Drug distribution/dispensing errors has been

reduced from 0.25 to 0.018% in semi-automated carousel system, while by using two days cabinet filling procedure errors has been reduced to 0.71 to 0.026% [21].

2.3.4.3 Automated Pharmacy Carousel System

Automated Pharmacy Carousel system contains barcode medication bins and scanner, a label printer. This system interface carousel system with pharmacy information system of hospital by a software [25]. Study has investigated frequency of distribution errors in three scenarios. This system decreases the prescription errors from 1.6 to 0.6%. In a repeated studies, errors reduced even more i.e. 0.4% [25].

2.3.4.4 Computerized Drug–Drug Interaction Alerting System

Adverse effects of drugs are the significant cause of deaths and emergency cases in whole world. These adverse drug effects (ADEs) are due to drug-drug interaction. Therefore while preparing drugs, pharmacists should be careful. In order to avoid incidents caused by ADEs, an online system of drug-drug interaction alerting system is now in use [16].

A study has investigated usage of this online alerting system by physicists and pharmacists. Study has been done in three periods. In first period study showed that system was present in 40% pharmacies but no physician practices it. In second period, study showed that 90% of pharmacies were capable to use the system but only 40% pharmacists used it [21]. In final period, 95% of pharmacies have this system and among them 90% are taking advantage of this system. Study observed the dispensing errors in these three periods and concluded that errors reduced by 21% and 68% respectively in second and third period in comparison to the first [21].

3 DESIGN METHODOLOGY & SYSTEM MODELLING

3.1 Introduction

In previous chapter, purpose of identifying most occurring medical errors and hazardous effect was to design the basic architectural system that can eliminate those problem. In this chapter an overview of design methodology of the thesis has been described. By identifying specific problem statement discussed in literature review, a feasible model has been developed.

The structure of this chapter is as follow: section 3.2 presented solution for the significant effect of hazardous drugs, section 3.3 presented solution to the three classified areas of compounding errors and compares it to the present technologies, section 3.4 shows the characterization of the system in order to reduce distribution errors, section 3.5 summarizes the targeted goals of the system, section 3.6 contains system's model description.

3.2 Characteristics to Avoid Hazardous Effects of Drugs

Significant effects of hazardous effects have been discussed earlier in literature review. In order to address the adverse effects of different neoplastic agents, American National Institute for Occupational Safety and Health (NIOSH) and the International Society of Oncology Pharmacy Practitioners (ISOPP) regulated the use of Closed Transfer System, But according to a study even these closed transfer system do not completely eliminate the risks involved in handling hazardous drugs [7]. In this thesis, to ensure complete safety of healthcare providers, following characteristics have been added to the proposed dosage system;

3.2.1 Closed Transfer System:

The presented compounding and dosing system uses the closed transfer devices as per the definitions provided by (NIOSH) and (ISOPP). Design of these devices restricts the environmental microorganism to contaminate the product and also inhibit the hazardous drugs to come in contact with the environment. Compact design of closed transfer drug reduces the risk of skin contacts and accidental spills.

3.2.2 Occupational Hazard Controlled Design:

According to Food and Drug Administration (FDA), a regulatory organization of US, it is mandatory to prepare the hazardous drugs by taking care of certain protocols. Every pharmacist and nurse should comply with few procedures while handling these hazardous drugs. Firstly use gloves, respirators, gloves and lab coats and then work inside a laboratory hood to offer a barrier to possible risks of these antineoplastic agents and hazardous drugs [26].

Cross-contamination of NIOSH's hazardous drug classes, machine of this dosing and compounding system has been located in a compact design serve as a hood. This design makes system more compact in terms of mobility and also serves as a preventive barrier for the healthcare worker from hazardous cancer drugs.

3.2.3 Automated Work Routine:

After connecting the disposable closed transfer devices to the system, this compounding and dosing system has all automatized routines. Automation of the system reduces the effects of toxic formulation prescribed in chemotherapy, thus reducing occupational risks of these drugs to the healthcare practitioners.

3.3 Characteristics Focusing Compounding Errors

In literature review four themes of compounding has been discussed to achieve a successful drug compounding. Presented dosing system can achieve error free drug compounding by having following characteristics:

3.3.1 Barcode Medical Administration

Errors in identification of the medicines contribute a lot in medical accidents. This type of error can be occurred due to sound-alike or look-alike names of medicines. Therefore avoid such error, this system contains a barcode system. It has been already proven that barcode system reduce the medical errors from 0.19% to 0.07% in a year [24].

Database of approved drugs has been provided to the system. Barcode administration of this system enable the user to scan the drug in hand before usage and the name of medicine has automatically stored in the database of patient, records of the machine and also shown on the receipts. In this way any mistake that has been committed by the pharmacist in selecting the drug, can be taken in account at three stages:

- When name of the drug appears after scanning the barcode, pharmacist can realize the difference between the names of prescribed one and the scanned one.
- Receipt of the prepared drug contain name of the scanned drug and its barcode, which can be cross checked by the direct healthcare provider before dosing.
- Error in identification of the drugs can be proved even after the adverse effects appear. Name of the responsible pharmacist who prepared the dosage is always present in record across each drug preparation. Record contain name of the pharmacist, name of the patient, drug name, prescriber name and date and time. All this information is also present in the record of each patient.

3.3.2 Uncontaminated Environment

Second theme for a successful compounding has been assured closed transfer devices of the system. Moreover by providing a special designed hood to the system, ISO specified environment can achieve easily for each drug compounding. Closed drug system also ensures purity of the prepared drug to enhance quality of the process.

As this system mainly target the preparation of cancer drugs, therefore by this characteristic occupational hazards of antineoplastic agent can also be reduced.

3.3.3 Automated Calculations

Many compounding errors are due to the personnel activities like wrong calculation. Some errors are due to conversion between matric and decimal system.

In this system all the back end calculations are performed automatically by the software. Therefore the errors due to the wrong mental calculations can be eliminated. Usually pharmacists and nurses confuse the total vial content in milliliters with the concentration of the prescribed required. In order to solve this problem, this system contain an inbuilt calculation interface which enable the pharmacist to put desired concentration of the product, after pharmacist gives the mass mentioned on the source drug[1] total volume needed (in milliliter) has been automatically generated. This way it eliminates the possible calculation errors by the pharmacists and nurses.

[1] Source drug is the drug to be aspired, contained in the vial attached to the system.

3.3.4 Electronic Medication Administration Records (MARs)

Medical Administration record is a report saved by the hospital administration for legal issues. Manual administration record again leads to many discrepancies. Therefore the presented system of this thesis stores electronic medical administration record of each patient. This system has been provided with databases of patients, medicines and their barcodes, pharmacists/nurses and of prescribers. Different hospitals have different format of these record. This system contains information shown in table 3-1 to face any legal issue that can occur after any deliberate or unintentional errors:

Table 3-1: Format of Electronic Medication Record (eMAR)

Detail	Format
Administrative Detail	• Patient name • Patient residential number • Treatment detail
Prescription Details	• Drug name • Dosage amount(ml) • Dosage barcode • Frequency of preparation • Name of selected module (by which drug has been prepared) • Date and time of the compounding • Pharmacist/nurses ID (who prepared the drug) • Prescribing doctor details

3.3.5 Execution of Quality Plan

Last theme to ensure a successful compounding is to develop a control process for compounding. During compounding and drug preparation, nurses and pharmacists may miss several important steps. This problem needs execution of a specific quality plan.

This system contains a control process for execution of the quality plan. Graphical user interfaces, the guiding notes and caution messages compel user to adhere to a specific routine.

Thus a lot of compounding errors can be prevented from occurrence. Table 3-2 explains the action taken by the automated routine and the prevention of possible errors.

Table 3-2: Controlled Routine of Software and Errors Prevented

Actions	Preventions
User Specific Login	Blaming another user for an error
Patient ID Login	Dosage delivery to wrong patient
Display Recent Dosage History	Error in proceeding a wrong prescription
Automatic History Record	Deliberate changes in the history
Prescriber Information	Errors in prescription
Dosage Information	Errors in drug name, mentioning dosage amount (ml), scanning barcode, selecting preparation parameters like, frequency of preparation

3.4 Characteristics Focusing Distribution Errors

There are two main characteristics that address many distribution errors mentioned in literature review. These characteristics ensure delivering an error free medicine to the patient.

3.4.1 Controlled Software Routine

Following categories of distribution errors can be solved efficiently by controlled Software Routine of the presented system

- Distributing medicine for the wrong patient (or for the wrong ward)
- Distributing the wrong medicine
- Distributing the wrong drug quantity
- Distributing at the wrong time
- Distributing an expired or almost expired medicine
- Omission (i.e. failure to dispense)
- Distributing a medicine of inferior quality (pharmaceutical companies)

Patient login, barcode system, controlled user interfaces for quantity prescribed and saving date and time across every drug compound reduces the chances of first five errors mentioned above. Omission of an order has been cross checked by the patient history and history of machine. If an order has been proved to be prepared by the system, chances of omission will be sufficiently reduced. Last distribution error regarding inferior quality can be omitted by the updated drug database. Only approved drugs from the regulatory authorities have been added to the database and can be used by the system.

3.4.2 Customized Label Printing

System presented in this thesis print two customized labels after each drug preparation. Labels are also shown in Figure 3-1 and Figure 3-2

Label for prepared drug

Label for already used source drug vial

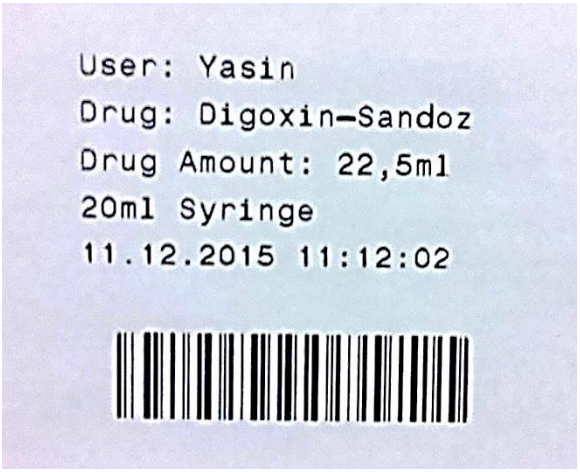

Figure 3-1:Label for Prepared Drug

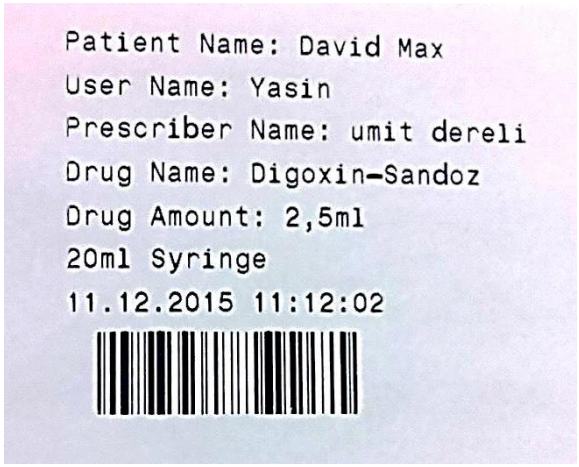

Figure 3-2: Label for Used Drug Vial

Detail of each label has been mentioned in Table 3-3:

Table 3-3: Customized Labels and their Details

Label	Details
For prepared drug	Name of Patient Name of User Name of Prescriber Drug Name Drug Amount Name of Channel Date and Time Barcode of the Drug
For already used source drug vial	Name of User Drug Name Channel Name (with which drug recently get used) Barcode

These customized labels prevent following distribution errors:

- Incorrect patient name
- Incorrect drug name
- Incorrect drug strength
- Incorrect user name
- Incorrect drug quantity
- Incorrect prescriber name
- Incorrect expiry date

3.5 Summarized Features of High-Precision Compounding and Controlled Dosing System for Occupational Hazardous Drugs

Design methodology of thesis has been developed by identifying most frequently encountered medical errors around the world. By applying all the characteristics presented earlier in this chapter, this system becomes capable of all the features shown in Figure 3-4.

Figure 3-3: Objectives of the System

Automatized routine reduces cycle time for each drug preparation with increased accuracy and the precision. The closed transfer devices insure safety of healthcare workers and the pharmacists. Active databases help to reduce many compounding and distribution errors. Additionally these databases are helpful in legal matters of health care. One of the target of this design was to make it economical reasonable so that there should be no remarkable trade-off between health safety and price of the system. Final product is a compact design. All of these features make it easy to use, economical reasonable to install and above all insure less medication error.

3.6 System Modelling

After finalizing the targets, system design and modelling is the most important step of research projects. Earlier in this subject all the characteristics of this system has been presented. Therefore achieve each one of them, a compact system has been modelled, which can be served as a complete solution to many compounding and distribution errors. In the figure 3-5 interfaces of complete unit system has been shown as a block diagram.

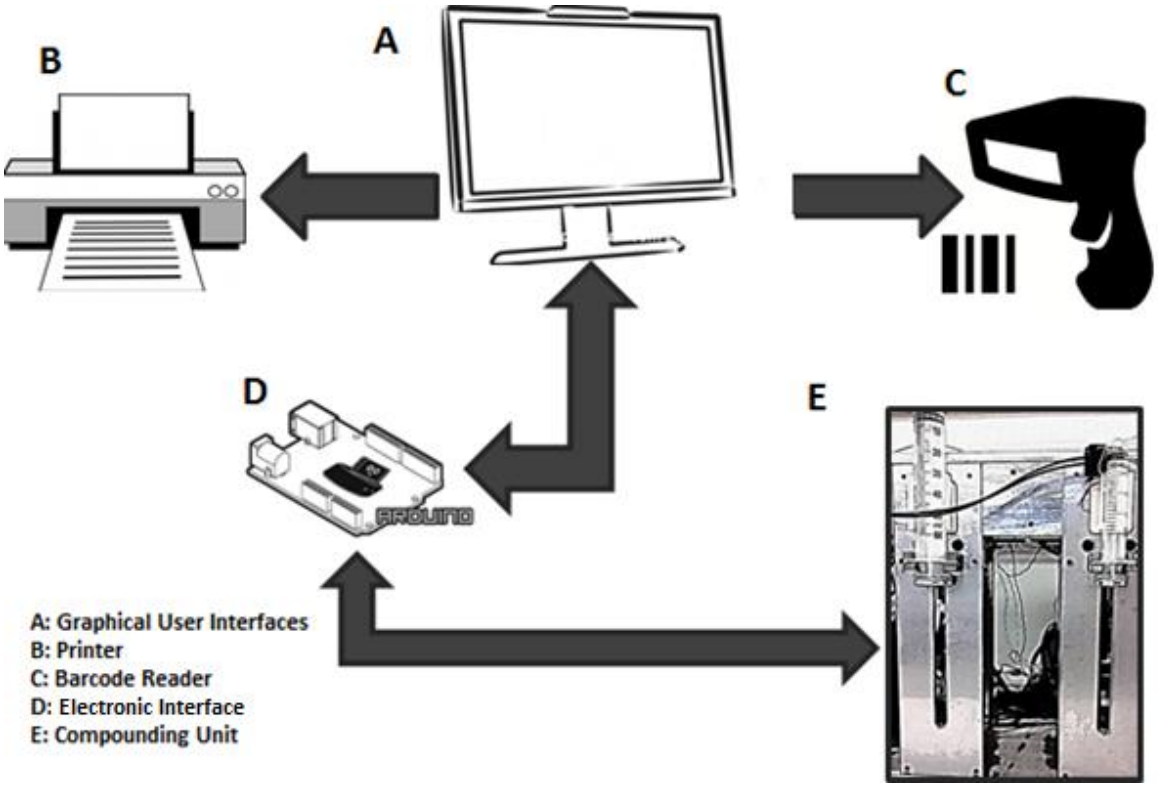

Figure 3-4: Block Diagram of High-Precision Compounding and Controlled dosing Design for Occupationally Hazardous Drugs

3.6.1 Compounding Unit

Compounding Unit has a modular design, having two channels for the drug preparation. One channel is capable to prepare medicine up to 60ml and other can prepare medicine up to 20ml only. User or pharmacist selects each channel based on the viscosity and desired quantity of the drug. Each channel has a servo drive, motor, ball screw assembly and syringe pump. This automated compounding unit works by filling syringe apparatus. Drivers of the compounding unit receive the inputted commands of the user and follow the instructions.

Details of the hardware of this unit can be found in section 4.2 and section 4.3.

3.6.2 Controller

Controller controls all the operations of the compounding unit. Programming of controller insures all the routines go accurately and precisely. It gets instruction from supervisory control and delivers to drivers of the compounding issue.

3.6.3 Graphical Unit Interfaces

Graphical user interfaces of supervisory control unit enable the pharmacists to adhere with a specific routine to reduce medical errors. These graphical interfaces are easy to use and thus reduce the cycle time of each drug preparation. In Manufacturing and Automation Research Centre this supervisory control consists of a touch screen computer, having visual studio installed.

3.6.4 Interfacing Devices

There are two interfaced devices that have been attached to this high-precision compounding and controlled dosing system. Following are the two modules:

- Barcode for Barcode Medicine Administration System
- Printer for Printing Customized Labels
- Camera

4 HARDWARE DESCRIPTION & ACCURACY ANALYSIS

4.1 Introduction

While developing high precision compounding and controlled dosing system, the main aim was to produce a compact, closed and highly accurate compounding and dosing system. Other than the interfaced devices like camera, barcode and printer, the final design contain three main parts.

- Graphical user interfacing device
- Compounding unit
- Controller

In this chapter mechanical, electrical and electronic hardware details of compounding unit and its electronic interfacing device has been described. Compounding unit is a bi-module device, having motor drives, servo motors and two ball screw assemblies.

In this chapter, section 4.2 describes the hardware details of the motor drives, section 4.3 explains the specification of ball screw assembly and servo motor, section 4.4 will give a detailed explanation about electronic interfacing of compounding unit, and section 4.5 presents detail accuracy analysis of the system and description of software coding and hardware settings to achieve a high-precision system.

4.2 Hardware Detail of Motor Drives

As it has been already mentioned that compounding unit is a bi-modular unit, therefore two servo motors drives are working for two different channels as shown in figure. Wiring, I/O and driver setting for both are same. This section will present details of wiring of the driver, power connections, description of input and output signal along with internal drive settings.

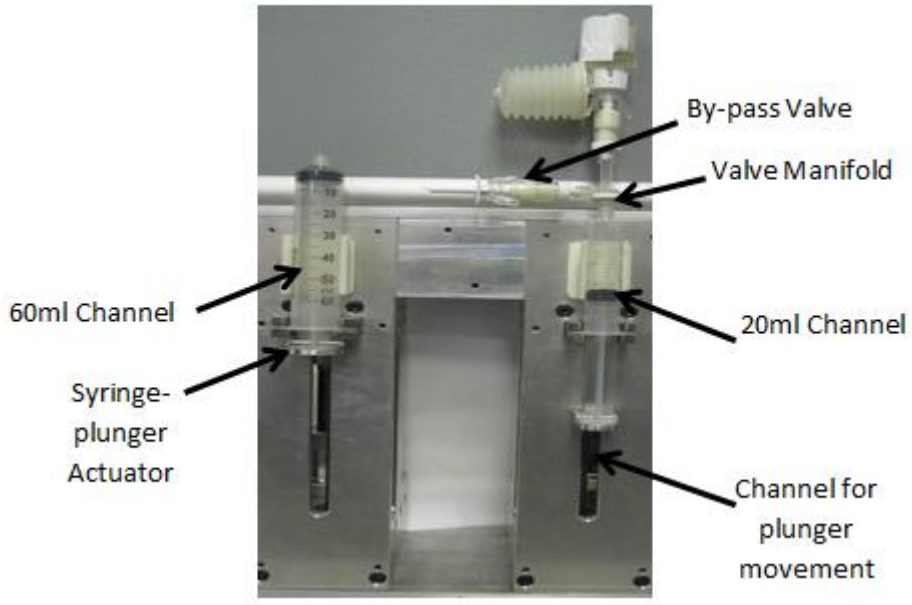

Figure 4-1: Bi-Modular Compounding Unit

4.2.1 Wiring Details

Driver used in the presented system contain following terminals

- **L1c, L2c Terminal:** This is a Control Circuit Terminal, and it is used to connect single phase AC control circuit power. This terminal uses equal voltage as the main circuit.
- **R, S, and T Terminal:** This is the Main Circuit Terminal which is used to connect single-phase or three-phase AC main circuit power depending on connecting servo drive model.
- **U, V, W, and FG Terminal:** This is Servo Motor Output which is used to connect with terminal op servo motor. There wires: U; the red wire, V; the white wire and W; the black wire are used to connect three phase servo motor main circuit cable. While FG; the white color wire, is used to connect servo motor with the ground terminal of motor drive.
- **CN1 Terminal:** This is an input and output connector which is used to connect driver with the external controllers.
- **CN2 Terminal:** This is an encoder connector, which is used to connect the drive with encoder of the motor.
- **CN3 Terminal:** This is a communication connector, which is used to connect driver with PC. This connection is helpful to change the setting of the driver by the relevant software of the driver.

- **CN4 Terminal:** This is a reserved connector.
- **CN5 Terminal:** This is analog voltage output terminal, which is used to monitor the operation status. The driver is provided with two channels MON1 and MON2 to output the analog data with the reference to the ground.

In figure 4-1 wiring diagram of driver has been shown. In the figure power-on is normally open contact and power-off is normally closed contact.

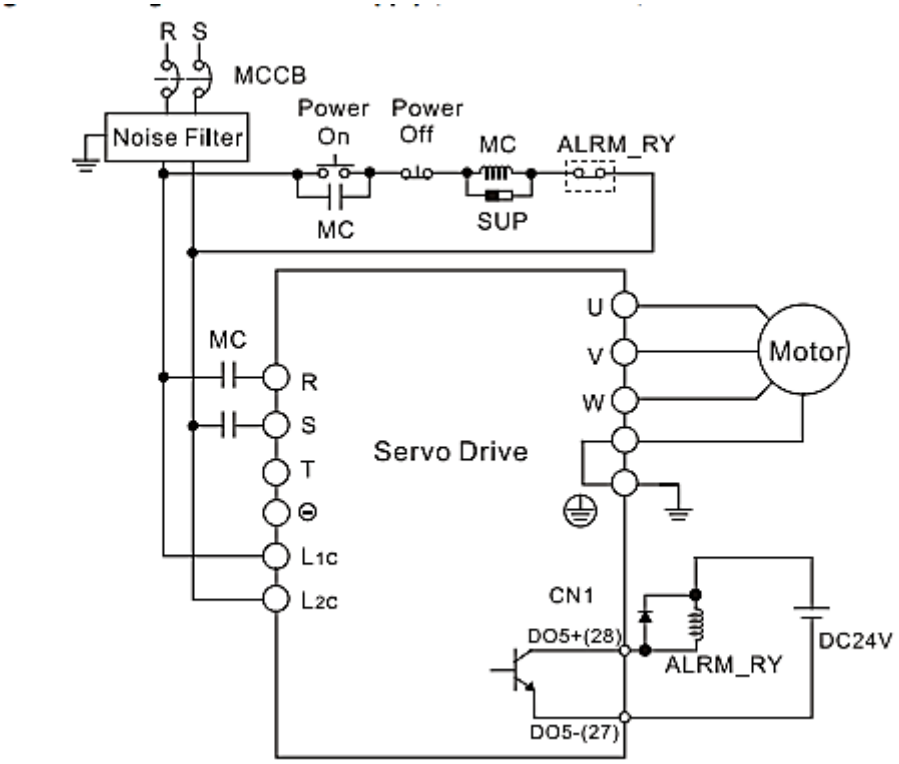

Figure 4-2: Single phase power supply [27]

4.2.2 Power Connections

In section 4.2.1, wiring details have been given for the single phase input power connection. Power connection to the servo drive includes control circuit terminal (L1c, L2c) and main circuit terminal (R, S, and T).

After the power turns on, the display on motor drives shows alarm “AL014”. If there is no text or character displayed on LED display than the voltage of control circuit terminal could be low.

4.2.3 Input / Output Interface Connections

There are three types of the signals that can be accessed by connecting the controller with CN1 terminal i.e. input/output interface connector. These three types of signals are mentioned below;

- General interface for :
    - pulse / direction inputs
    - encoder reference signal from the motor
    - the analog speed and torque control
    - reference voltages
- Digital Inputs: There are 8 programmable digital inputs.
- Digital Outputs: There are 5 programmable digital outputs.

Therefore understand required input and output interfaced connections following topics have been discussed here in details:

- CN1 Terminal Identification
- Explanation of Interfaced Signals
- Wiring Diagram of Pulse Input

4.2.3.1 CN1 Terminal Identification:

Figure 4-2 shows the layout of input/output interface connector.

Figure 4-3: The Layout of Connector CN1 [27]

Figure 4-3 shows the pin configuration of CN1 connector. Pins that need to be connected with controlled have been highlighted. Detail of these pin has been given later in this section.

1	DO4+	Digital output
2	DO3-	Digital output
3	DO3+	Digital output
4	DO2-	Digital output
5	DO2+	Digital output
6	DO1-	Digital output
7	DO1+	Digital output
8	DI4-	Digital input
9	DI1-	Digital input
10	DI2-	Digital input
11	COM+	Power input (12~24V)
12	DI9-	Digital input
13	OZ	Encoder Z pulse Line-driver output
14	COM-	VDD(24V) power ground
15	DO6-	Digital output
16	DO6+	Digital output
17	VDD	+24V power output (for external I/O)
18	T_REF	Analog torque Input
19	GND	Analog input signal ground
20	V_REF	Analog speed input (+)
21	OA	Encoder A pulse output
22	/OA	Encoder /A pulse output
23	/OB	Encoder /B pulse output
24	/OZ	Encoder /Z pulse output
25	OB	Encoder B pulse output
26	DO4-	Digital output
27	DO5-	Digital output
28	DO5+	Digital output
29	GND	Analog input signal ground
30	DI8-	Digital input
31	DI7-	Digital input
32	DI6-	Digital input
33	DI5-	Digital input
34	DI3-	Digital input
35	PULL HI	Pulse applied power
36	/HPULSE	High-speed position pulse (-)
37	/SIGN	Position sign (-)
38	HPULSE	High-speed position pulse (+)
39	SIGN	Position sign (+)
40	/HSIGN	High-speed position sign (-)
41	/PULSE	Pulse input (-)
42	HSIGN	High-speed position sign (+)
43	PULSE	Pulse input (+)
44	OCZ	Encoder Z pulse Line-driver output

Figure 4-4: CN1 Terminal Signal Identification [27]

4.2.3.2 Explanation of Interfaced Signals

Table 4-1 shows the detail of all interfaced signals that have been highlight in figure 4-3.

Table 4-1 Explanation of Interfaced Signals

Signal		Pin Number	Detail
Position Pulse Input	**PULSE**	43	Three different pulse commands can be selected via parameter P1-00. Quadrature, CW + CCW pulse & Pulse / Direction. In this system Pulse/Direction command has been selected. Details of this selection have been given in c part of this section.
	/PULSE	41	
	SIGN	39	
	/SIGN	37	
	PULL HI	35	
Power	**VDD**	17	COM+ is the common voltage rail of the Digital Input and Digital Output signals. Connect VDD to COM+ for source mode. For external applied power sink mode (+12V to +24V), the positive terminal should be connected to COM+ and the negative to COM-.
	COM+	11	
	COM-	14	
Power	**GND**	19	The polarity of VDD is with respect to Ground (GND).
	SON	9	Servo On. Switch servo to "Servo Ready".
	ARST	33	A number of Faults (Alarms) can be cleared by activating ARST.
	CCLR	10	When CCLR is activated the setting is parameter P2-50 Pulse Clear Mode is executed.
	EMG	30	It should be contact “b” and normally ON or a fault (ALRM) will display.

4.2.3.3 Wiring Diagram of Pulse Inputs

There are two strategies for the pulse input signal.

- Line driver input; Maximum frequency of signal for line driver input is 500kpps.
- Open-collector input; Maximum frequency of signal for open-collector input is 200kpps.

In this thesis, drivers get open-collector pulse input. Wiring of such input has been shown in figure 4-5.

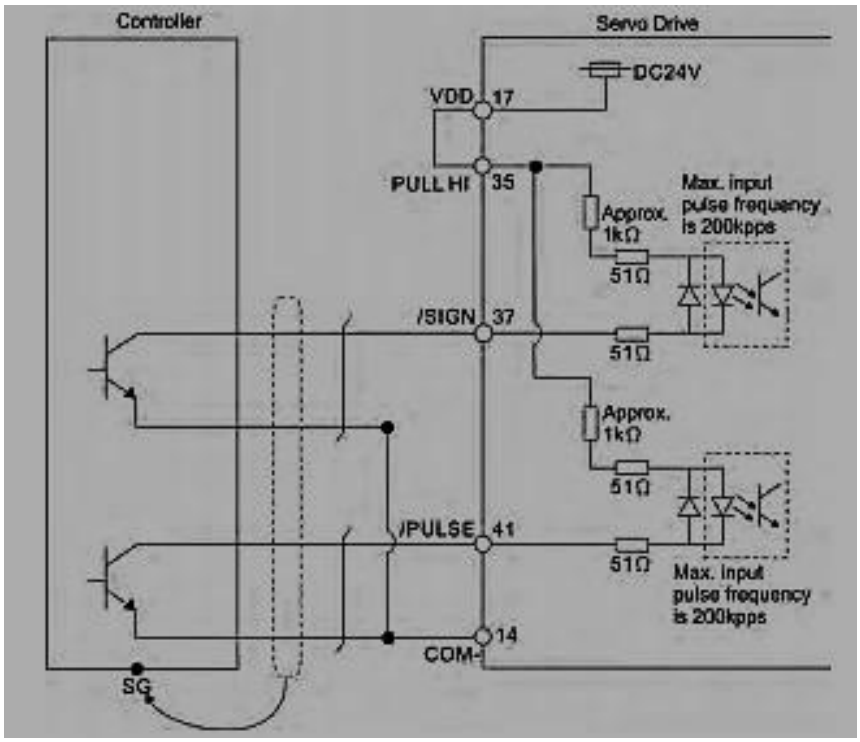

Figure 4-5: Pulse Input for Internal Power Supply [27]

4.2.4 Internal Driver Settings

4.2.4.1 Digital Keyboard and Setting Display

Internal driver settings can be changed manually by digital keypad, having a digital display and function keys. Digital keypad of the drivers used in presented compounding unit has been shown in figure 4-6.

Figure 4-6: Description of Digital Keypad

Before knowing what parameter should be set, a technician should know about the keys of digital keypad and their function. Table 4-2 shows names of the keys and their corresponding functions.

Table 4-2: Keypad Keys and their Functions

Name	Function
LCD Display	The LCD Display (5-digit, 7-step display panel) shows the monitor codes, parameter settings and operation values of the AC servo drive.
Charge LED	The Charge LED lights to indicate the power is applied to the circuit.
MODE Key	MODE Key. Pressing MODE key can enter or exit different parameter groups, and switch between Monitor mode and Parameter mode.
Shift Key	SHIFT Key. Pressing SHIFT key can scrolls through parameter groups. After a parameter is selected and its value displayed, pressing SHIFT key can move the cursor to the left and then change parameter settings (blinking digits) by using arrow keys.
Up and down Key	UP and DOWN arrow Key. Pressing the UP and DOWN arrow key can scroll through and change monitor codes, parameter groups and various parameter settings.
Set Key	SET Key. Pressing the SET key can display and save the parameter groups, the various parameter settings. In monitor mode, pressing SET key can switch decimal or hexadecimal display. In parameter mode, pressing SET key can enter into parameter setting mode. During diagnosis operation, pressing SET key can execute the function in the last step.

After setting drivers internal parameter by pressing set key will automatically save the setting. But if digital display shows some of the characters shown in table 4-3 then there will be some

reasons that are preventing the settings to be saved. Table 4-3 also shows the description of each error that might come across.

Table 4-3: Save Settings Displays [27]

Display Messages	Description
	Parameter's setting value has been saved
	Some parameters cannot change if the servo is on. For them this caution message can appear.
	Invalid password or no password was input.
	The setting value is error or invalid.
	This parameter is read only. Write-protected.
	This parameter is valid after restarting the drive

4.2.5 Position Control Mode (PT)

Position control mode is mostly use for the high precision applications. Therefore to achieve highly accurate compounding unit, position control mode has been selected among speed control and torque control. Therefore set the control mode as a position control mode, parameter P1-01 should be set on the value of 00.

Now system will accept an external command for the positioning of motor. This command has been executed by DI signal.

4.2.5.1 Command Source of PT

Command source of position control mode can be changes according to inputted pulses by changes parameter P1-00. Figure shows the settings for parameter P1-00;

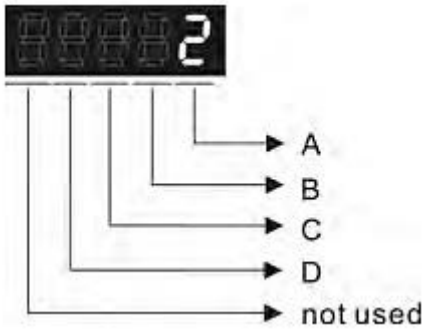

Figure 4-7: Settings for Control mode parameter P1-00

A: Input pulse type

0: AB phase pulse (4x) (Quadrature Input)

1: Clockwise (CW) + Counterclockwise (CCW) pulse

2: Pulse + Direction

3: Other settings:

Selected Option for A:

2: Pulse + Direction

B: Input pulse filter

Selected Option for B:

4. Default value, as no filter is required for input signal.

C: Input polarity

Selected Settings for C:

Positive Logic of pulse polarity has been selected.

D: Source of pulse command

Selected Value for D:

As open collector input pulse interface has been already selected therefore setting value for D of P1-00 will be 0.

Table 4-4: Settings for pulse Command

Setting Value	Input Pulse Interface	Remark
0	Open collector for low-speed pulse	CN1 Terminal Identification: PULSE, SIGN
1	Line driver for high-speed pulse	CN1 Terminal Identification: PULSE_D, SIGN_D

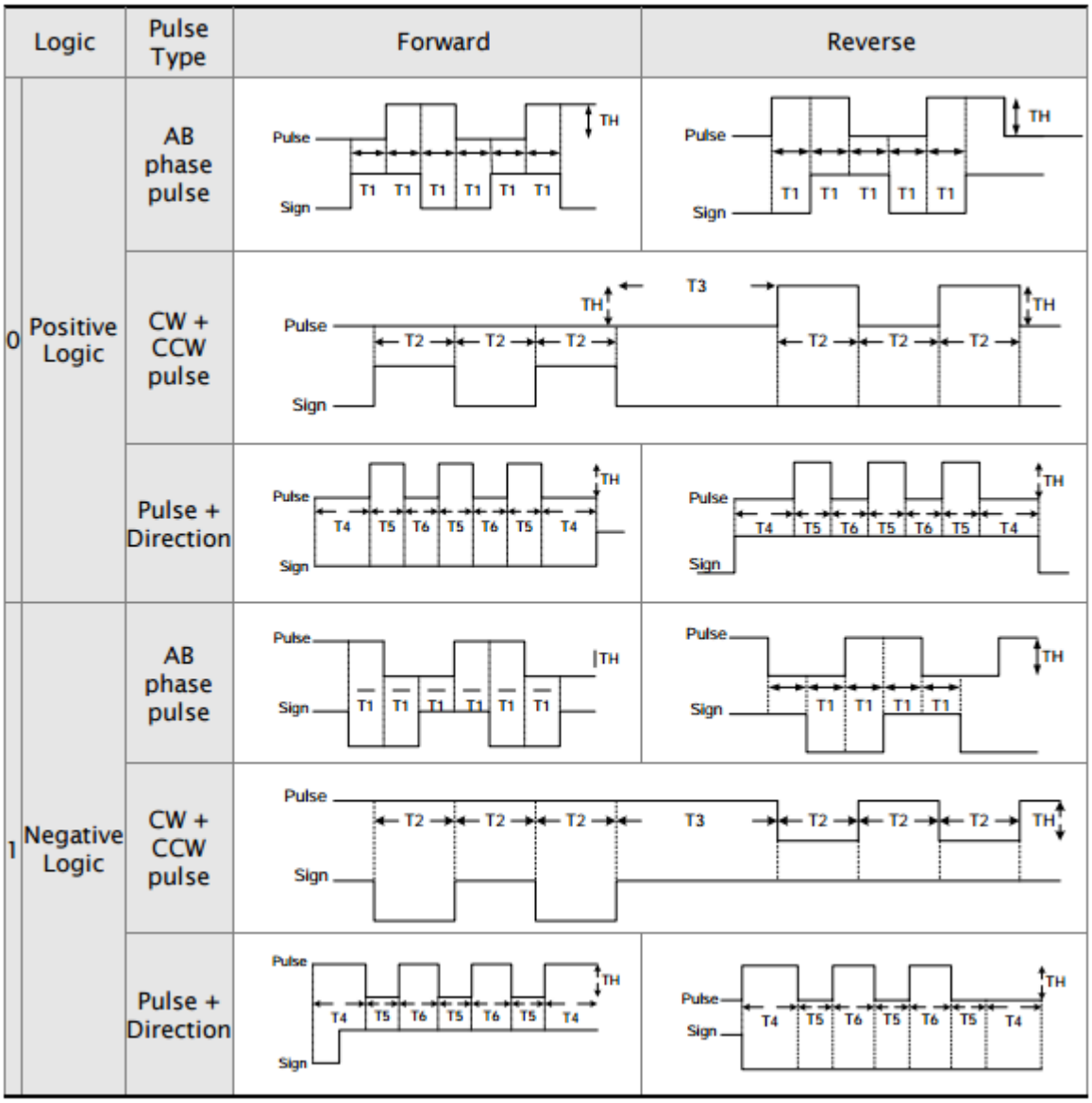

Figure 4-8: Input Polarity Settings [27]

4.2.5.2 Electronic Gear Ratio

Electronic gear ration will help to control travel distance change. But if parameter of denominator and nominator are out of range that can cause motor to run chaotically. Even within the range very high electronic gear ration will cause motor to run unsmooth.

- Relevant Parameters for Electronic Gear Ratio
    - **P1-44 Electronic Gear Ratio (1st Numerator) (N1):** This parameter has been allocated for numerator of electronic gear ratio.
    - **P1-45 Electronic Gear Ratio (1st Denominator) (D1):** This parameter has been allocated for numerator of electronic gear ratio.

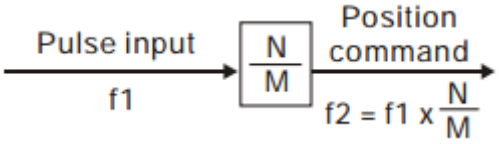

Figure 4-9: Electronic Gear Ratio of Drive

- Limit for Electronic Gear Ratio

Electronic Gear Ratio setting range must be within: 1/50<25600.

- **Selected Values for Electronic Gear Ratio**

Value for N/M i.e. P1-44/P1-45 has been set as 128,000/10, so that drive can take 100 pulses from controller for one revolution:

4.3 Hardware Details of Ball Screw Assembly:

The ball screw drive is a mechanism that converts rotary motion into linear motion and vice versa. It consists of a lead screw and a nut made of channels in which precision balls circulate in the spaces of screw. Due to precision balls circulating between nut and lead screw it provides low friction coefficient. The efficiency of ball screw drive is greater than conventional lead screw drives roughly up to 90 %. Also the load distribution and stress factor is low as the load is equally distributed in to the balls.

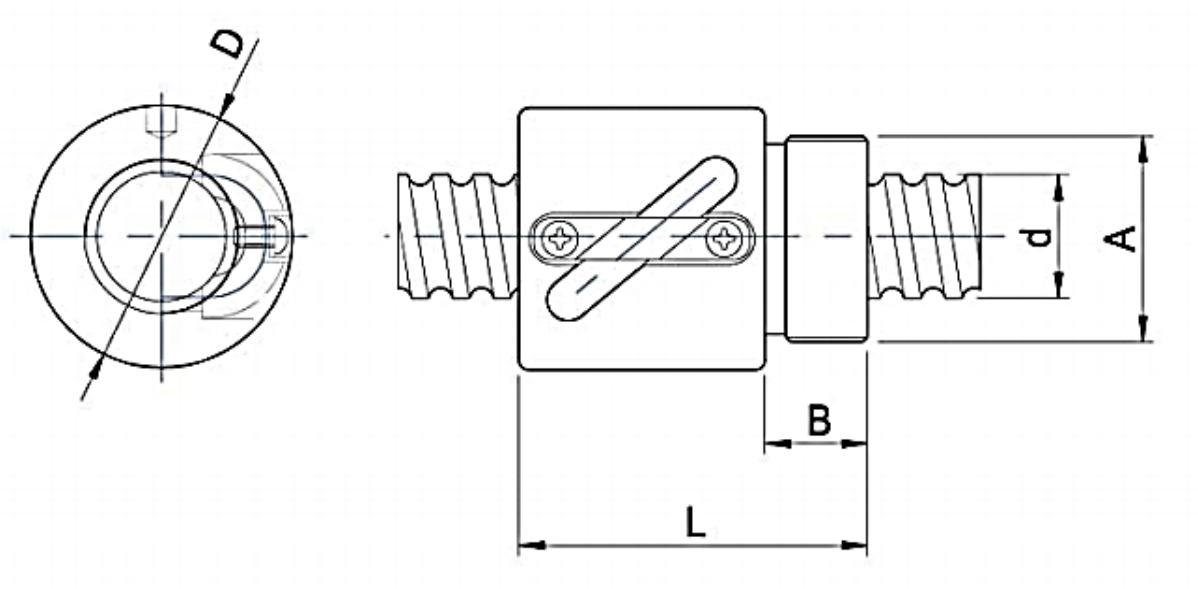

Figure 4-10: Ball Screw Schematic

Ball screw drive is used in this project to convert rotary motion from ac motor in to linear motion of plunger. The specification of ball screw unit is listed below.

Table 4-5: Specifications of Ball Screw Assembly

Model No.	**Screw Size**		**Ball Diameter (mm)**	**Basic Rate Load**	
	O.D (mm)	Lead **(mm)**		Ca Dynamics (Kgf)	Co Static (Kgf)
1204	12	4	2.381	425	738

Lead is the distance travelled by nut in one revolution of screw. The lead or travel accuracy is very important factor in high precision drug delivery. Lead is defined in product data sheet but supplier usually do not provide percentage error or in lead. Therefore in order to make sure the accurate and precise drug delivery, accuracy test has been conducted in the lab using precision laser displacement sensor.

4.4 Electronic Interfacing Device

There is one electronic interfacing device that controls both 20ml channel drive and 60ml channel drive. This device has been interfaced serial with the main supervisory control. Supervisory control sends commands to the embedded microcontroller in this device. Microcontroller segregates the position command as number of pulses, and the direction command as the sign and forwards both commands to the drives. Both drives cannot be activated at same time. Decision of selection of drive has been made on supervisory level. Then by sending a specific byte serially the decision is transferred to microcontroller. And microcontroller send PULSE And SIGN signal to the respective drive.

Figure 4-5 shows the electronic circuitry of device. In this figure CMD1 and CMD4 signals each connecting with NPN transistor 2N3904 are the /PULSE and /SIGN signals for driver of 20ml Channel. This arrangement has been already mentioned as Open Collector Input Signal in previous sections. Similarly CMD2 and CMD3 signals each connecting with NPN transistor 2N3904 are the /PULSE and /SIGN signals for driver of 60ml Channel.

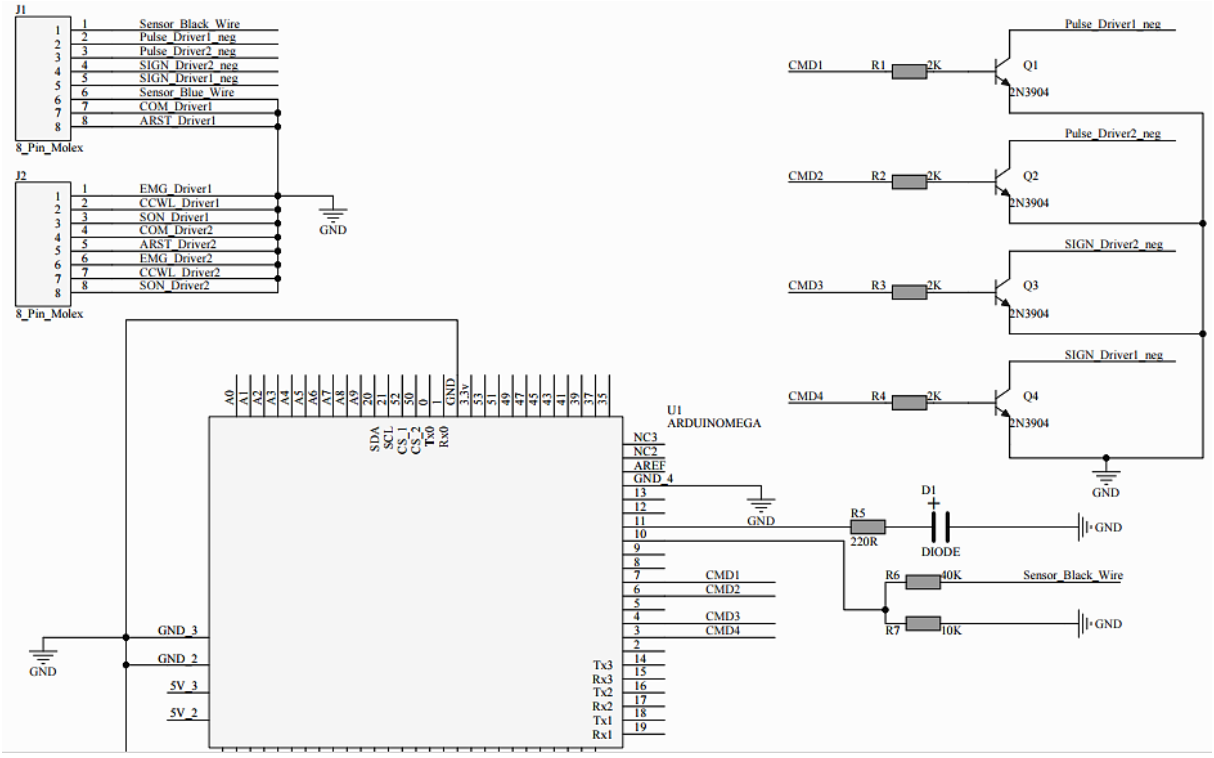

Figure 4-11: Electronic Circuitry of Interfacing Device

Diode D1 has been replaced by an EMERGENCY STOP button. Now if during operation user press emergency stop button, /PULSE signal do not proceed to the drive and operation get hanged. System will come back to its offset position by a reset GUI button from supervisory control. This will make system get ready for new command.

In figure 4-11 PCB design of electronic interface device has been shown.

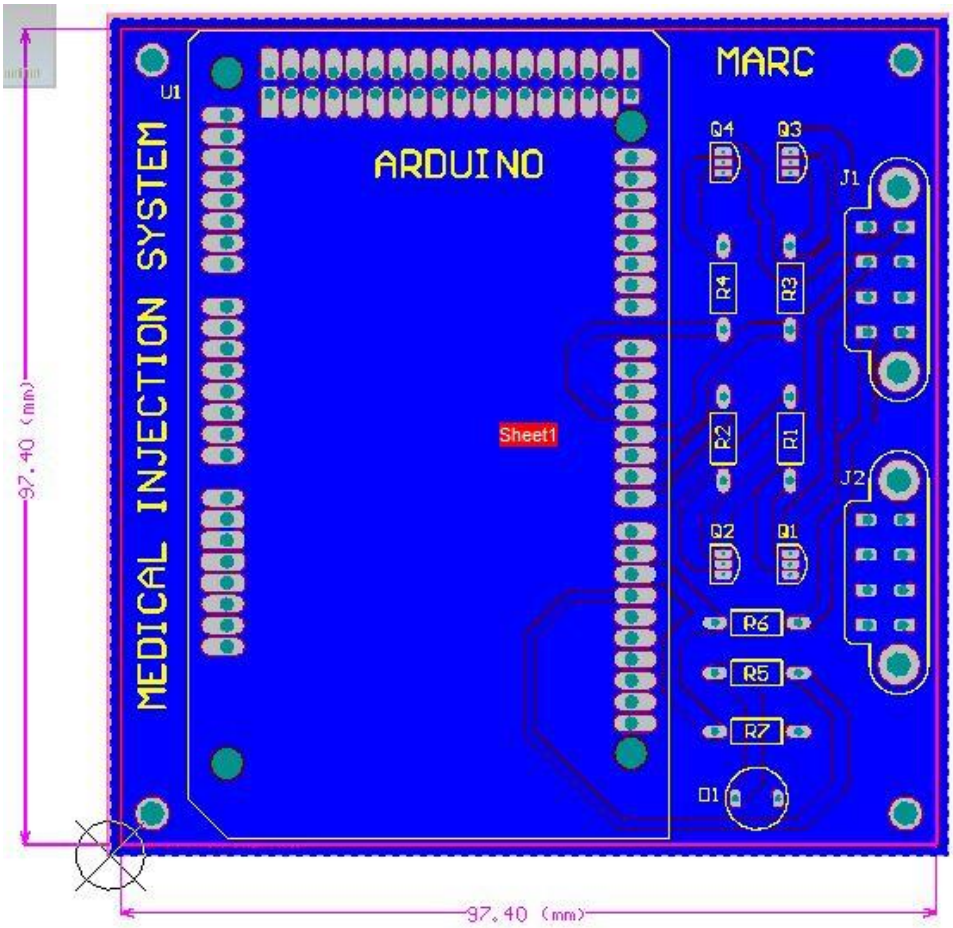

Figure 4-12: PCB Design of Electronic Interfacing Device

4.5 System Performance Analysis

This section evaluates the accuracy of the High-Precision Compounding and Controlled Dosing System. System performance analysis has been done in following two majors steps;

1. Accuracy Analysis of the Hardware
2. Accuracy Tests and Results

4.5.1 Accuracy Analysis of the Hardware

A modern electronic solution and microprocessor solution along with back end software coding has improved the accuracy of the systems. In this section, the accuracy of the system's hardware has been analyzed in following two sub-sections;

- Supervisory Control to Mid-Level Control Accuracy
- Mid-Level Control to Low-Level Control Accuracy

4.5.1.1 Supervisory Control to Mid-Level Control Accuracy

Graphical user interfaces in the supervisory control have the back end coding that cares of double-precision floating number. These floating numbers are mentioned as amount to be prepared. This amount is transmitted to the mid-level supervisory control. And software take cares of double-precision number. And microprocessor receives exact command of amount serially as send by the user.

4.5.1.2 Mid-Level Control to Low-Level Control Accuracy

At the mid-level control, amount of the drug to be prepared is processed by the microprocessor coding and is transmitted to motor drives. Accuracy of hardware has been analyzed by considering following factors:

a. Electronic Gear Ratio
b. Theoretical Pitch of Ball Screw Assembly
c. Calculation of Theoretical Pulses per ML (milliliter)
d. Accuracy of Ball Screw Assembly by Laser Sensor
e. Calculation of Actual Pulses per ML (milliliter)

a. Electronic Gear Ratio

Electronic gear ration gives simple ratio change of travel distance. Setting high electronic gear ratio can cause the position command to act like a stepped command. In those situations low-pass filters should been used by setting proper parameters described in section 4.2. Electronic gear ratio of motor drives in this system has been set by following parameters;

$$f2 = f1 \times N/M$$

$f1 = Command\ Pulse\ Input,\ f2 = Position\ Command\ of\ motor\ drive, \frac{N}{M} = Electronic\ gear\ ratio$

Therefore 100 Pulses per Revolution can be achieved by setting electronic gear ration as follow;

$$1280{,}000 = 100 \times 128{,}000/10$$

$$100\ pulses = 1\ Revolution$$

b. Theoretical Pitch of Ball Screw Assembly

Theoretical pitch of the ball screw in section 4.3 has been mentioned as 4mm. Therefore travel of the system on 100 pulses should be 4mm. Ball screw assemblies of both channels

have same specifications. But to analyze actual hardware accuracy of the system, travel of ball screw assembly has been found experimentally in below section.

c. Calculation of Theoretical Pulses per ML (milliliter)

Pulses required to prepare one milliliter has been found by following calculations;

$$Volume\ (mm^3) = \pi \times \frac{D2}{4} \times Pitch\ of\ Ball\ Screw\ Assembly \tag{4.1}$$

For Channel having 20ml Syringe

$$Volume = \pi \times \frac{(19.13mm^2)}{4} \times 4mm$$

$$Volume = 1149.686\ mm^3$$

$$Volume = 1.1497\ ml$$

In order to find number of pulses per milliliter;

$$100\ pulses = 1.1497ml$$

$$86.9 \cong 87\ pulses = 1ml$$

For Channel having 60ml Syringe

$$Volume(mm^3) = \pi \times \frac{(26.7mm^2)}{4} \times 4mm$$

$$Volume = 2239.609\ mm^3$$

$$Volume(ml) = 2.23961\ ml$$

In order to find number of pulses per milliliter;

$$100\ pulses = 2.23961ml$$

$$44.65 \cong 45\ pulses = 1ml$$

d. Accuracy of Ball Screw Assembly by Laser Sensor

Accuracy of the pitch has been found by the laser sensor. By assembling laser sensor with each of the channel, actual travel in 100 input pulses has been calculated.

- **For Channel having 20ml Syringe:**

Laser Sensor Displacement

$$1ml\ = 3.37mm$$

$$87pulses\ = 3.37mm$$

$$100\ pulses\ = 3.873mm$$

Therefore actual pitch of ball screw of 20ml channel, founded by laser sensor is 3.873mm instead of 4mm.

- **For Channel having 60ml Syringe:**

Laser Sensor Displacement

$$1ml\ = 1.752mm$$

$$45\ pulses\ = 1.752mm$$

$$100\ pulses\ = 3.893mm$$

Therefore actual pitch of ball screw of 60ml channel, founded by laser sensor is 3.893mm instead of 4mm.

e. Calculation of Actual Pulses per mL (milliliter)

Below are the calculations of pulses required per milliliter for both channels, depending upon actual pitch of ball screw assemblies found by the laser sensor.

For Channel having 20ml Syringe

By using equation 4.1;

$$Volume(mm^3) = \pi \times \frac{(19.13mm)2}{4} \times 3.873mm$$

$$Volume = 1113.184\ mm^3$$

$$Volume = 1.1131\ ml$$

In order to find number of pulses per milliliter;

$$100\ pulses = 1.1497ml$$

$$89.83 \cong 90\ pulses = 1ml$$

For Channel having 60ml Syringe

By using equation 4.1;

$$Volume(mm^3) = \pi \times \frac{(26.7mm^2)}{4} \times 3.839mm$$

$$Volume = 2149.465\ mm^3$$

$$Volume = 2.149\ ml$$

In order to find No. of Pulses per ML;

$$100\ pulses = 2.23961ml$$

$$46.53 \cong 46\ pulses = 1ml$$

Therefore by sending resultant pulses for each milliliter, this system gets even more accurate results.

4.5.2 Accuracy Tests and Results

4.5.2.1 Methodology

In order to find accuracy of system's fluid dispensing unit, a series of accuracy tests have been conducted. For efficiently gauging the accuracy and precision, compounding and dosing system has been used by following to protocol mentioned in user guide from chapter 7. For each of 20 ml syringe and 60 ml syringe, 10 samples have been prepared for each volume, from 3ml to 20ml and from 20ml to 60ml respectively.

Protocol of Data Acquisition

1. Place the container on the scale.
2. Tare the scale.
3. Perform desired volume suction from source vial.
4. Attach the container to output adopter.
5. Inject the medicine in the target container.
6. Place container on the scale.
7. Record weight of the container, mention speed of preparation and the name of channel used.

4.5.2.2 Data Omission:

Some data points have been omitted due to following reason. Calculations have been made without these omitted data points.

- **Personal Error**: Personal errors can be due to many factors, like mistake in assembling valves and manifold accurately according to user guide and measurement errors due to not following data acquisition protocol properly.
- **Greater Degree Inaccurate Data Points**: Those data points which were variating a lot actually deemed the technician error, malfunction of the valve and manifold connectivity, or non-compliance to the data acquisition protocol. It is also possible that scale was not properly tared before preparation of drug.

4.5.2.3 Results

Accuracy tests have been done 10 times for each volume from 3ml to 20ml. For 60ml syringe, 10 samples have been prepared for every multiple of 5 from 20 ml to 90ml. Average accuracy has been concluded by calculating average error for each volume, then average of all errors has been taken for both 3ml-20ml and 20ml-60ml. average accuracy has been found by subtracting calculating average error from cent percent. The difference of desire value to the average actual value has been taken for each volume. Then by taking averages of differences from ranges 3ml-20ml and 20ml-60ml give accuracy specification of each channel.

Table 4-6: Accuracy Results

Measurement Range	3 to 20 mL	20 to 60 mL
Count	180	90
Average Accuracy	93.7%	98.8%
Accuracy Specification	±0.56ml	±0.388ml

Percentage Error of 20mL and 60mL Syringe:

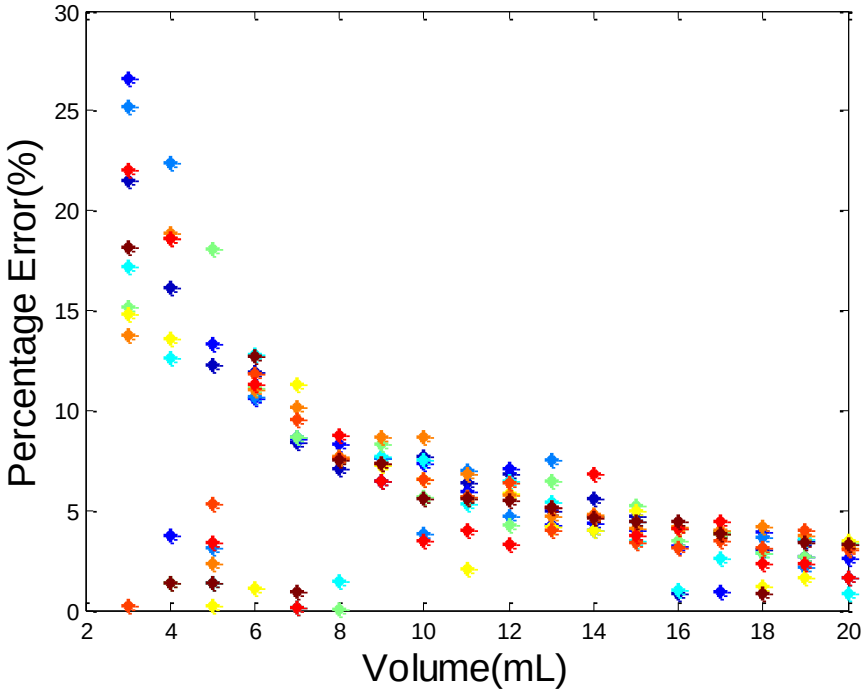

Figure 4-13: Comparison of Volume (mL) with Percentage Error (%) of 20ml Syringe

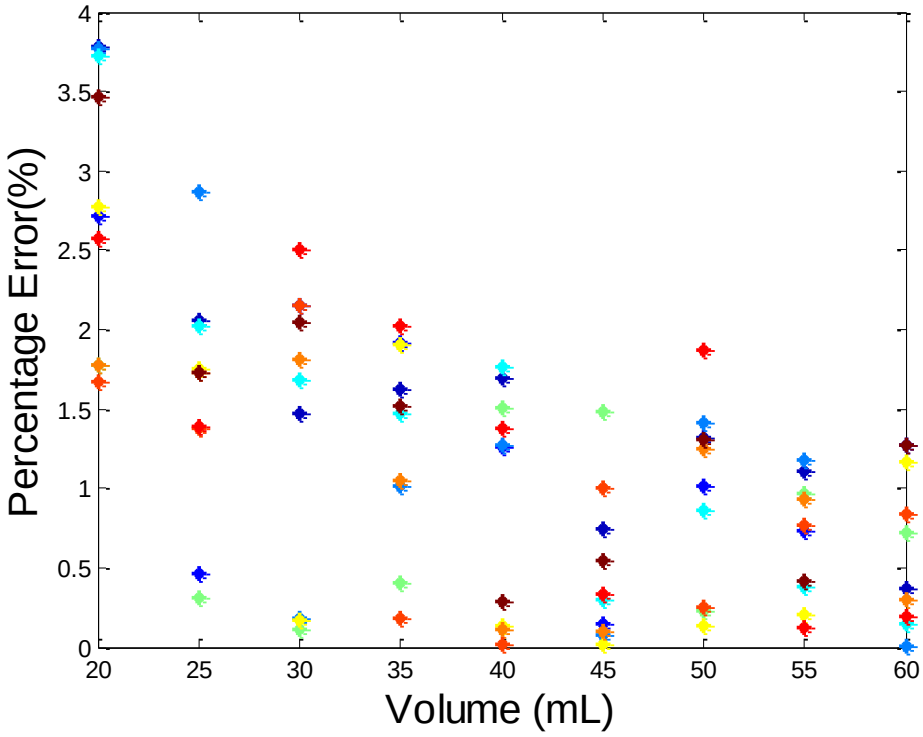

Figure 4-14: Comparison of Volume (mL) with Percentage Error (%) of 60ml Syringe

Actual Volume vs Desired Volume for 20ml and 60 Syringe:

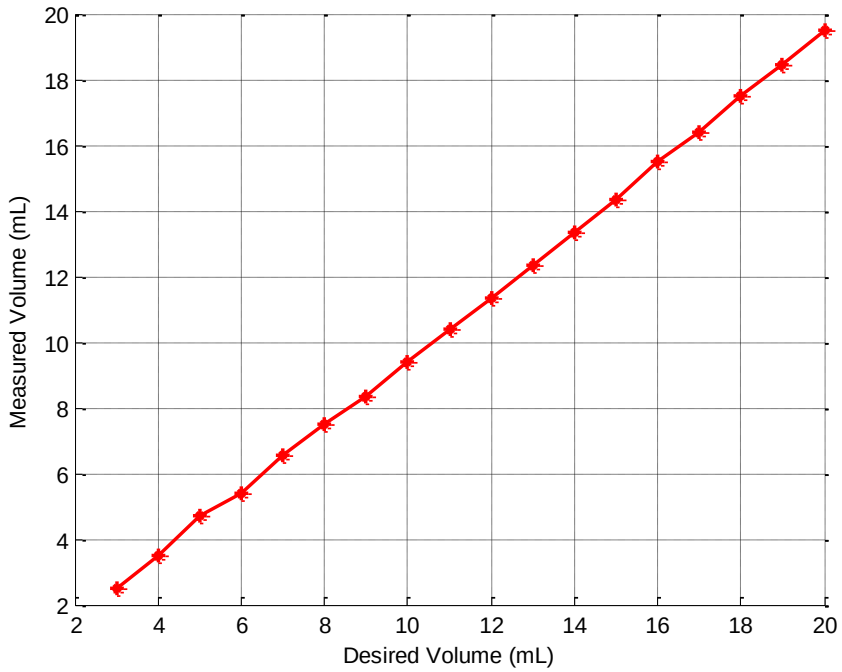

Figure 4-15: Comparison of Desired Volume to the Measured Volume of 20mL Syringe

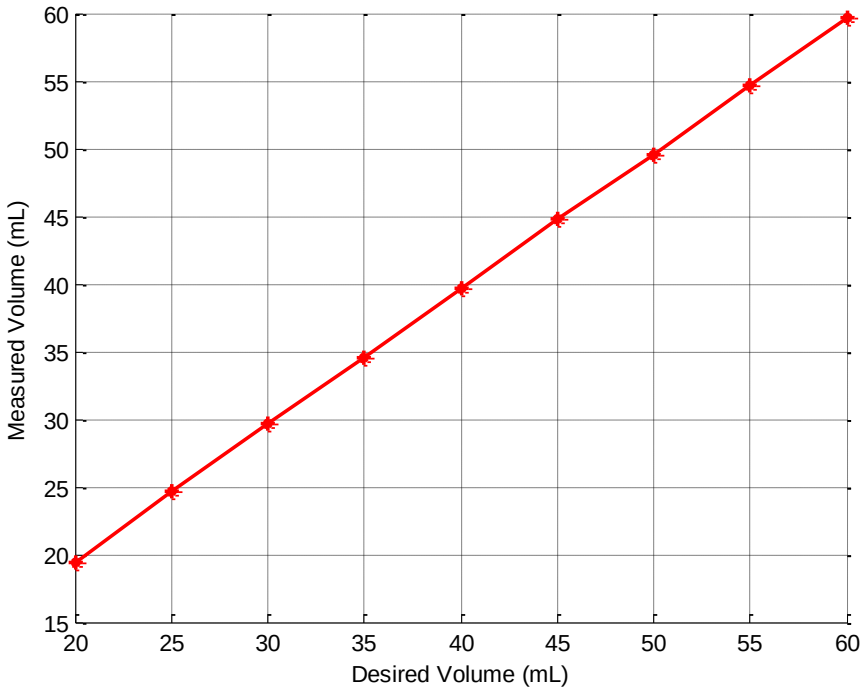

Figure 4-16: Comparison of Desired Volume to the Measured Volume of 60mL Syringe

5 SOFTWARE DEVELOPMENT

5.1 Introduction

After the hardware design, the most important milestone in development of any automated system is software development. Software of high precision compounding and controlled dosing system is not only controlling the hardware of the system but it contains many controlled interfaces for a quality dosing routine. Software of this system control the position input of drives depending upon the command given by the user[1]. There are three levels of control; Low-level control (drives), Mid-level control (electronic interface device) and supervisory control (Graphical user interface). By segregating respective jobs to all these three levels, high precision of the system has been achieved.

Software of this system is not only controlling the hardware devices but it also includes other features than that. In second chapter there were many problem statements that have been discovered after intensive study on medical errors. In order to avoid all those situation in which a nurse or pharmacist can commit any mistake; a quality plan needs to be define. In chapter three, methodology to achieve a successful compounding and dosing process has been defined. In order to implement the methodology, software has been developed in such a way that it not only serves as a control commander of the hardware but also adhere the user to follow a quality routine toward a successful error free compounding and dosing of drug.

In this chapter, section 5.2 describes the software detail of low-level control, section 5.3 will give detail software routine of Mid-level control and pseudocode, section 5.4 describes software detail of supervisory control, last section gives details of dosing design, its flow chart and design development.

5.2 Software Details of Low-Level Control

Motor drives are at the lowest level in control hierarchy. Section 4.2.4 gives the guidelines for settings the parameters of the drives. For parameter P1-01, the selected value is 00 that runs the drive on principle of position control mode. In this mode, drive receives two different signals from the electronic interface device. One of them is /PULSE and other is /SIGN. Each of two drives of compounding unit receives these two inputs from the interfacing device, one at each time.

Basic control structure of position control mode is given in figure 5-1;

[1] Pharmacists or nurses who use the system

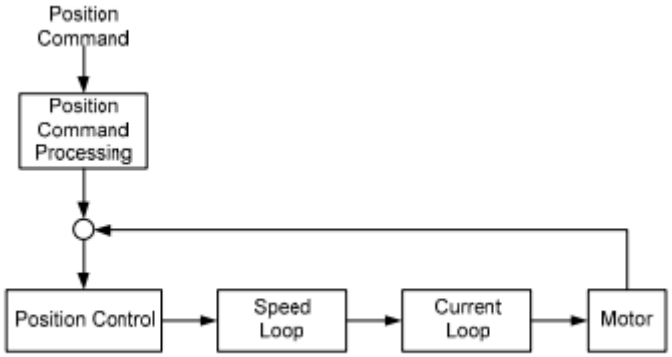

Figure 5-1: Control Structure of Position Control Mode [27]

Position command has been send by microcontroller of electronic interfacing device. This command then process in position command processing unit of drive. After processing unit a command has been generated according to electronic gear ratio of the drive. This command controls the position, speed and current for operation of the motor.

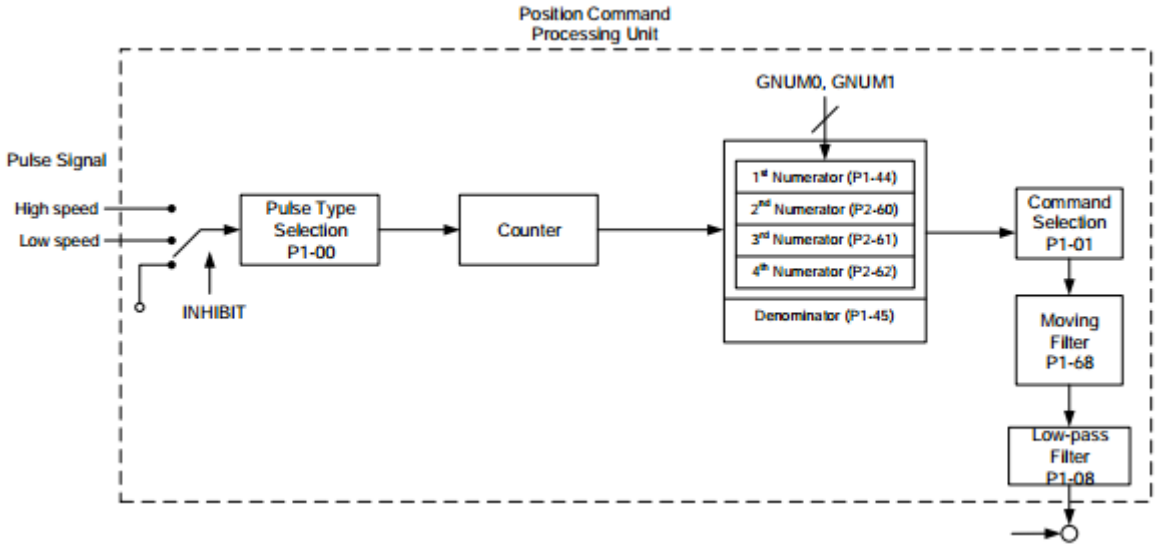

Figure 5-2: Position Command Processing Unit

Figure 5-2 shows details of position command processing unit. In compounding unit both drives has parameter P1-00 set as pulse type of PULSE/ DIRECTION. When PULSE and SIGN signal reaches the position command processing unit, then P1-00 selection mode help drive to recognize it as pulse and direction. After going through pulse counter and incorporating electronic gear ratio factor, drive decide the control mode of operation. Selected setting for P1-01 in drives is set as position control mode. This mode specifies pulse specification according to set parameters. Due to selected settings shown in section 4.2.4, input pulse has following specifications:

- Maximum input frequency : 200Kpps
- Voltage specification: 24V Max.
- Forward specification: < 25mA

5.3 Software Details of Mid-Level Control

Mid-level controlling has been performed by the embedded microcontroller in the electronic interface device. This Microcontroller receive data serially form the supervisory control. After that a define program get executed and as a result microcontroller give commands to the low level control.

5.3.1 Receiving Serial Data from Supervisory Control

Supervisory control is sending data serially, stored in a ten byte sized buffer. Details are given in section 5.4.2. At level of microcontroller this data has been received by following code.

```
void setup() {
Serial.begin(57600);
}
void loop() {
 Index=0;   // initialize a do loop to receive buffer send by VS it will run until index is 9. index is from 0-9
 do
 {
  if (Serial.available() > 0)
 {
  incomingByte = Serial.read(); // serially read and store data in a variable for each buffer
    buffer[index]=incomingByte; //variable is assigned to another variable
    ack=1;
    index++;  //increment index from 0 to 9
 }
 }while(index != 10);
```

Baud rate of serial port should match the baud rate of serial port mention in supervisory control. After saving incoming byte coming serially in to the buffer [index], each index of buffer transmit one command from supervisory control to the microcontroller program routine.

5.3.2 Transmitting Commands to Low-Level Control

After command get saved in each buffer index, these values help to decide which routine of program should be executed. Main understanding can be gained by the piece of code below. Detail programming is given in Appendix A.

```
void setup()
{
  // initialize the digital pin as an output.
 pinMode(pulse, OUTPUT);
 pinMode(dir, OUTPUT);
 pinMode(pulse1, OUTPUT);
 pinMode(dir1, OUTPUT);
}
```

These four output pins of microcontroller are attached to the four inputs of NPN transistors. Collectors of these NPN transistors are the inputs of drives. Two inputs of each drives include one signal for PULSE and one signal for SIGN/DIRECTION. Detailed electronic circuit has been shown in figure 4-10.

5.3.3 Pseudocode of Microcontroller Programming

Below is the pseudocode of microcontroller programming. Details program is in Appendix A.

```
START
PROGRAM<INFUSION_SYSTEM>
Void Setup();
(
    Open Serial Port;
    Declare Inputs and Outputs;
)
```

```
Void Loop();
(
      Receive Serial Data;
     WHILE( Index=10);
DO
    BufferIndex = Serial Data;
ENDWHILE;
IF (Channel1 is Selected)
   PULSE = PULSE1;
   SIGN = SIGN1;
   Assign Pulse per ML accordingly
ENDIF
IF (Channel2 is Selected)
{  PULSE = PULSE2;
   SIGN = SIGN2;
   Assign Pulse per ML accordingly
ENDIF;
IF(User pressed START)
    Fill();
ENDIF;
IF(User pressed INJECT)
   Inject();
ENDIF;
IF(User pressed RESET)
   IF (A-B >0)
      Reset();
   ENDIF;
ENDIF;
   Fill();
IF (EMG =0)
 FOR (Until count = Amount)
     Set SIGN High;
    Set PULSE High;
   Set PULSE Low;
```

```
  B = Count;
ENDFORLOOP;
ENDIF;

Void Inject();
IF (EMG =0)
   FOR (Until count = Amount)
       Set SIGN Low;
       Set PULSE High;
      Set PULSE Low;
       B = Count;
   ENDFORLOOP;
ENDIF;

Void Zero();
  Amount = C;
  FOR (Until count = Amount)
  Set SIGN Low;
  Set PULSE High;
  Set PULSE Low;
  ENDFORLOOP;
ENDIF;
```

5.4 Software Detail of Supervisory Control

Supervisory control consists of user interfacing software. This interface enable user to communicate with the motor drives via microcontroller. In this thesis, software has been built in visual studio C# programming. Graphical user interfaces has been built in Window Form Application.

5.4.1 Serial Communication with Mid-Level Control

For serially communication of supervisory control with micro-controller, following steps have been taken;

- Microcontroller has been attached through USB-port of the supervisory computer.

- Note COM port of microcontroller by checking in Control Panel → Device Manager → PORTS (COM & LPT)
- Place a serial port from toolbox of supervisory control software.

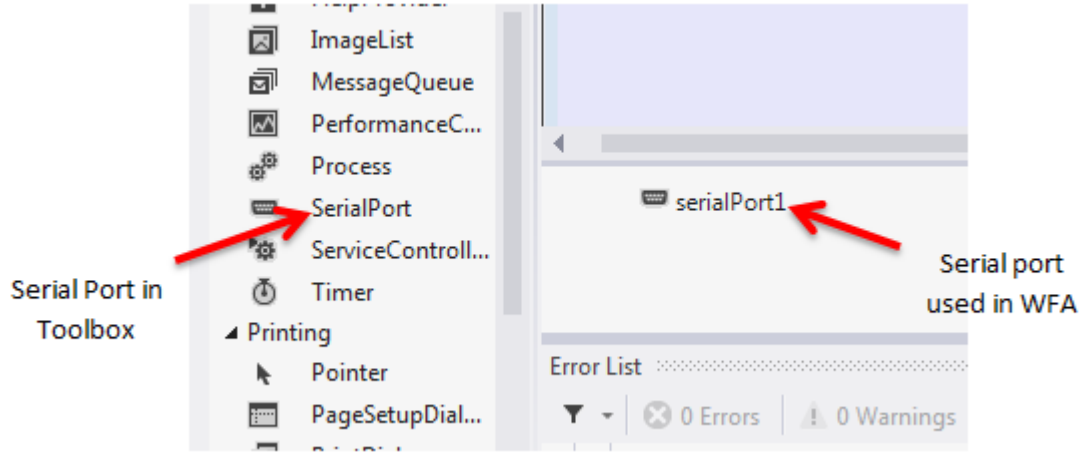

Figure 5-3: Using Serial port in Window Form Application

- By clicking on serial port interface, the properties can be shown as figure 5-3. Following settings are important for serial communication:
  - **Baud Rate:** Baud rate of serial port in visual studio should match the baud rate mentioned in serial port of microcontroller.
  - **Port Name:** Port name should be the one with which microcontroller has been attached.

(Name)	**serialPort1**
BaudRate	**57600**
DataBits	8
DiscardNull	False
DtrEnable	False
GenerateMember	True
Handshake	None
Modifiers	Private
Parity	**Space**
ParityReplace	63
PortName	**COM9**
ReadBufferSize	4096
ReadTimeout	-1
ReceivedBytesThreshold	1
RtsEnable	False
StopBits	One
WriteBufferSize	2048
WriteTimeout	-1

Figure 5-4: Properties of Serial Port Interface

5.4.2 Programming to Send Commands Serially

Serial data has been send by supervisor control to microcontroller of mid-level control. Initially a buffer of ten byte has been defined, after this each byte has been assigned by a decimal number that lie within range of 8 bits.

After assigning the buffer with corresponding command variables, next command will be executed to check whether serial port is open or not. If it is not open, next command will open it. And send ten values of buffer on the serial port. If processor can't find electronic interface device or microcontroller attached with the port it will give a caution message.

5.4.3 Commands Send by Supervisory Control

Below are the commands that supervisory control sends to the microcontroller in order to control performance of the compounding unit.

5.4.3.1 Amount of Drug to be Prepared

User puts required volume of drug in a textbox. Value in that textbox could be saved as integer and can send by a byte across serial port. But chemotherapy and some other medication needs micro liter volume of the drug while compounding. Therefore to make it possible, user should also be able to send a floating number as an amount to microcontroller. Floating number is more than 8 bits that is why two bytes should be allocated to transport the value of a floating number.

Then both these 8 bits variables have been assigned to two bytes and have been sending to microcontroller serially.

5.4.3.2 Speed of Operation

There are three variable speeds that can be selected by the user depending upon the viscosity of the drug. If viscosity is increases then the lower speed is recommended. User selects each of the high, medium and slow speed. Each selection will save a separate value in the speed variable. When supervisory control sends this variable serially, then the microcontroller will decide the amount of delay between each pulse according to the received command.

5.4.3.3 Channel Selection Command

It has been already described in chapter 3 that compounding unit is a bi-modular unit. It contain two channels, one is capable to prepare drug up to 20 ml and other is able to prepare the drug up to 60ml. Selection of each channel by user will allocate a special value to the

variable. And when microcontroller receives this value it will decide which channel user want to use.

5.4.3.4 Start Command

This command is used to start the operation of aspiration. When user presses the button 'START' a buffer containing this command will be transmitted serially. It will be received by microcontroller and in turn start transmitting PULSE and DIRECTION pulses to each drive to make it rotate counterclockwise and thus plunger of the syringe will be pulled down and aspire the drug from source vial.

5.4.3.5 Inject Command

This command is used to start the operation of Injection. When user presses the button 'INJECT' a buffer containing this command will be transmitted serially. It will be received by microcontroller and in turn start transmitting PULSE and DIRECTION pulses to each drive to make it rotate clockwise and thus plunger of the syringe will be pushed upward and inject the drug to the source bag.

5.4.3.6 Reset Command

This command is used to reset the compounding unit. When an emergency stop button has been pressed due to any emergency and thus stopped the motors in the half way of operation, then there will be the need of resetting the electronic interfacing device. That can be done by pressing this button. When rest command has been send by supervisory control, microcontroller send command to drives to reset its position at the zero position.

5.5 Dosing Routine Design and Development

Most of the problem statements explained in literature review needs efficient software for an automated device. Following are some medical errors that occur very frequently in hospitals. If pharmacist/nurse goes through a controlled procedure of dosing he/she has no chances to commit any one the following error.

- Distributing medicine for the wrong patient (or for the wrong ward)
- Distributing the wrong medicine
- Distributing the wrong drug quantity
- Distributing at the wrong time
- Distributing an expired or almost expired medicine

- Omission (i.e. failure to dispense)
- Distributing a medicine of inferior quality (pharmaceutical companies)

Detailed explanation about how controlled routine dosing system can inhibit all above errors is given in section 5.5.2. In the end of preparing each medicine two customized labels come out of printer. These customized labels prevent following distribution errors:

- Incorrect patient name
- Incorrect drug name
- Incorrect drug strength
- Incorrect user name
- Incorrect drug quantity
- Incorrect prescriber name
- Incorrect expiry date

Below sections contain flow diagram of controlled dosing routine and its screen shots with explanation.

5.5.1 Flow Chart

In figure 5-4 flow chart of dosing system has been shown that elaborate controlled routine of the system. Each user of the system has each login, by entering through that he/she can enter into system routine to prepare a drug according to quality drug dosing plan. This software routine keeps the user to adhere with routine shown in figure 5-4. Therefore any pharmacist or nurse cannot miss to mention even minor information. Additionally, user has to login the patient for whom he/she is preparing drug, this will prevent user to commit any mistake in mentioning wrong patient name on the label. Other than patient and user login, there is one more password authentication stage i.e. technical access. For any kind of trouble shooting or to access machine history to deal with any legal issue, technical person from the company can go through this access. Other details of interfaces will be given in section 5.5.2.

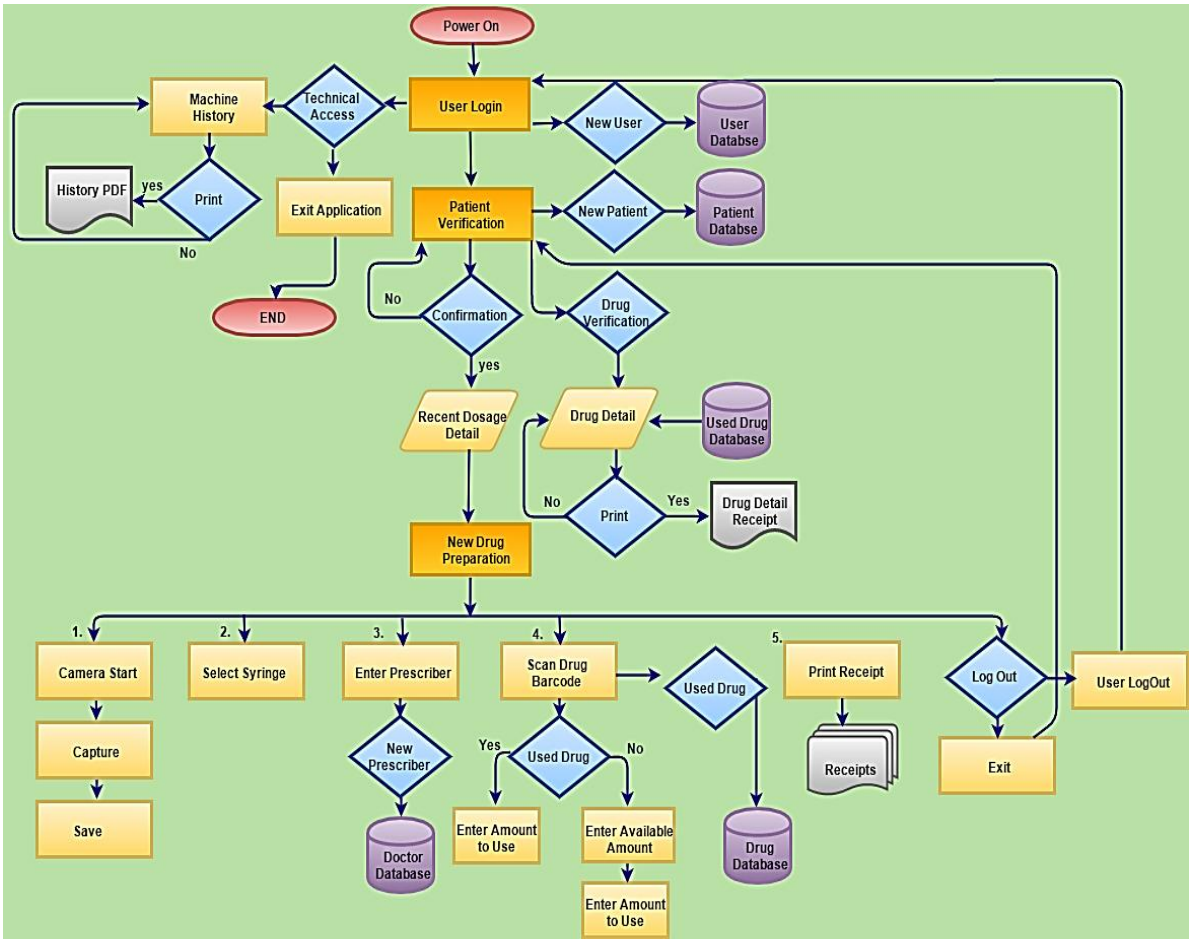

Figure 5-5: Flow Chart of Controlled Routine of Dosing System

5.5.2 Graphical User Interfaces of Dosing Routine

This section will demonstrated all the user interfaces of high-precision compounding and controlled dosing system step by step to make dosing routine understandable.

5.5.2.1 Language Option

Presented system has been built to first target the medical market of Turkey. Therefore this system interface has been developed in two languages; English and Turkish. For language translation this system used Add-in of Multi-Language in Visual Studio. Thus, this application can be translated into any language present in this add-in. While translating this application, add-in use to translate by online translators but for error proofing, translated list has been exported, cross checked, corrected and then imported back in the software.

When user Power-ON the application of the system, he/she came across with the language option as shown in figure 5-5.

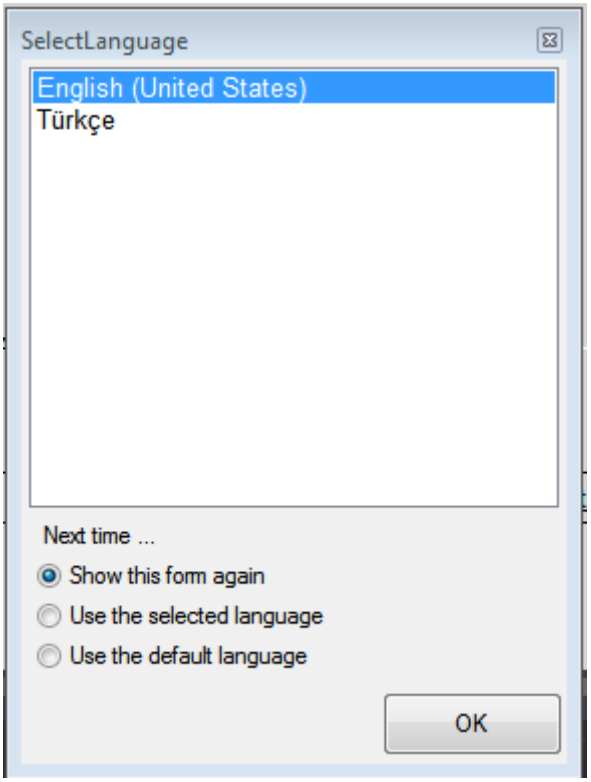

Figure 5-6: Language Options

5.5.2.2 Login

Next screen is of user login. In system application user login has been added for following main reasons

- Only authorized people can use the system
- Identity of user should be safe for claiming any legal issue

In interface shown in figure 5-6, user has to provide his/her login ID that is provided by the hospital/pharmacy management. User needs to provide password and then he/she can proceed forward by pressing button “Login”. Details of user’s login ID and password are saved in user information database.

Button Interface of Technical Access is limited to use for the technicians of the manufacturing company and cannot be access by user of the system. This technical access will proceed with requirement of batch no. and password of machine known to the company’s personals only.

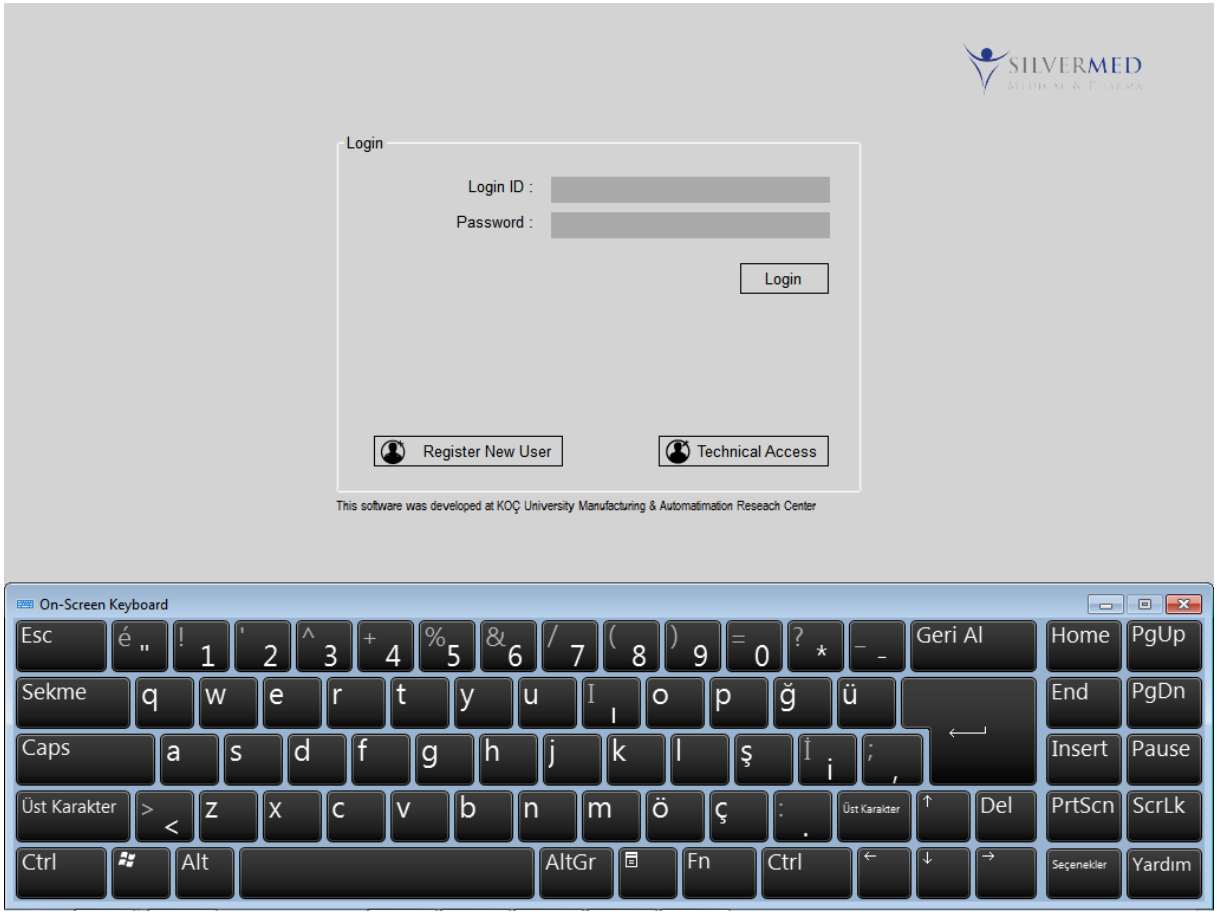

Figure 5-7: User Login Screen

5.5.2.3 Register New User

If a new user needs to be added in the users' database, he/she need to be register by the form shown in figure 5-7. Required fields of form are User Name, Login ID i.e. provided by the hospital/pharmacy management, password. Then user has to confirm the password to get register in the database of users of the system.

By clicking interface button "OK" one can be registered in database after passing through following few checks:

- All fields should be filled.
- Login ID should be unique, should not be already present in the database.
- Password and confirmed password should match.

Figure 5-8: Register New User Screen

5.5.2.4 Home

After user login interface, screen shown in figure 5-8 will be displayed. This interface has following three options to proceed forward:

- **Login Patient:** User clicks this interface if he/she wants to prepared new drug specific to a patient.
- **Verify Drug:** There are some source drugs which can be reused, for these source drugs this application creates a new label. If user wants to verify this drug he/she can verify it through this interface.
- **Logout:** If user wants to go back screen and wants to logout he/she can press this interface button.

In normal drug preparation routine, logged in user clicks patient login to prepare a new drug.

Figure 5-9: Home Page

5.5.2.5 Patient Login

If user in home screen chooses the option of patient login he/she comes across the interface shown in figure 5-9. At this step user needs to decide whether he want to prepared medicine for already registered patient or he first want to register a patient. Depending on requirement he will choose any one procedure to proceed.

- If patient is already registered, user puts patient's hospital ID/residential number in the mentioned field. And press "OK". Database displays the name of patient for confirmation of the patient. If name and hospital/residential ID both match to the prescription, user clicks confirm. If name of patient on display screen do not match with prescription that user needs to try again. Because user might commit a mistake in writing residential ID.
- If patient is not registered, user clicks on button interface of "Register New Patient". And after registering, do the steps mentioned in above procedure.

Figure 5-10: Patient Login Screen

5.5.2.6 Register New Patient

If patient on the prescription has not been registered into system database, user needs to add this patient before preparing drug for that patient. In order to register a patient, user need to mention the name of patient, patient hospital ID, nationality and the treatment. If patient is a Turkish citizen his hospital ID should be his residential number. Then user click on button interface of "Register New Patient". After going through following three checks patient get registered in the system database.

- All fields should be filled.
- Turkish citizen should have 11 digits residential number.
- Hospital ID should not be already present in the database.

After confirming all the necessities, patient gets registered and screen of patient login gets appear.

Figure 5-11: Register New Patient Screen

5.5.2.7 Detail of Recent Dosage

When user enters the login of patient, a screen containing information of patient recent or previous dosage appears. This step has been added to routine of the drug dosing for following reasons:

- In order to avoid dual dosage of same medicine.
- In order to check amount of recent medication before preparing new one for the patient.
- Prescriber name of previous medication is mentioned. Therefore if new prescriber prescribe another dose, a pharmacist/nurse can ask previous prescriber to confirm the authority of new one.

This screen has three options; Back: if user wants to cancel drug preparation of logged in patient, New Drug Preparation: If user wants to decide new preparation of logged in patient, View Patient History: If pharmacist/nurse wants to see whole previous history of patient.

Figure 5-12: Detail of Previous Dosage of Patient

5.5.2.8 New Drug Preparation

This is the main new drug preparation interface. For this system application prompts the screen shown in figure 5-12. When user clicks on "New Drug Preparation" interface of previous section, this screen appears. User has to go through following steps to prepare a new drug for a patient.

1. User has to "START" button to start camera routine, "CAPTURE" to capture the image of source drug vial. And finally save it by pressing "SAVE".
2. User has to select a channel between 20ml syringe and 60ml Syringe, depending upon the amount of dosage.
3. Patient name has been automatically appeared on the screen. It is name of the logged in patient.

Figure 5-13: Interfaces for New Drug Preparation

4. User has to select prescriber's name. If user cannot find prescriber name in drop down list, he/she needs to add the prescriber in system database. This can be done by clicking "ADD PRESCRIBER" button.

5. After mentioning the Prescriber's information and drug's information, user presses button "START" to suck the drug from the source container/vial.
6. After progress bar shows 100% complete process, button interface "INJECT" will appear. When user press this button, plunger inject drug in to target container.
7.
8. After this user has to put drug's detail, for this first of all he/she needs to scan the barcode of the drug. If name of the drug do not appear in the field of drug name, then the possibility is drug is not present in the drug database. For this possibility drop down the list of medicines. If user cannot find name of medicine it means that he/she needs to register the medicine before use. If name is present but scanning barcode do not make it appear in the field then do troubleshooting step (refer to section 8.1.2)
9. In order to register the medicine user need to press "UPDATE DRUG LIBRARY" button.
10. If user wants to update a drug library by importing an authorized drug list in excel format, he/she can import drug list by pressing "IMPORT DRUG LIBRARY".
11. After scanning the barcode, user need to mention available drug in the source vial of drug. Available amount must be given in unit of milliliter.
12. User needs to mention needed amount of source vial drug for the preparation of new drug. User can also put prescribed mass of the drug by mentioning the concentration of drug. After that user presses "CALCULATE" button to fill the field of amount in milliliters.
13. After mentioning name, available amount and required amount user needs to mention the speed of drug preparation. Speed should be selected depending upon the viscosity of drug.

5.5.2.9 Print Summary

When drug has been prepared, user has to press print summary to print the labels/receipts. After pressing the button screen shown in figure 5-13 can be seen. Although there are many options like saving receipt in XML, and export it as image, but in routine user presses "PRINT" button. On pressing print button a print dialog will appear. Choose language of printer. Language of printer attached to the system is EPL. After selecting the printer name, user prints the receipt.

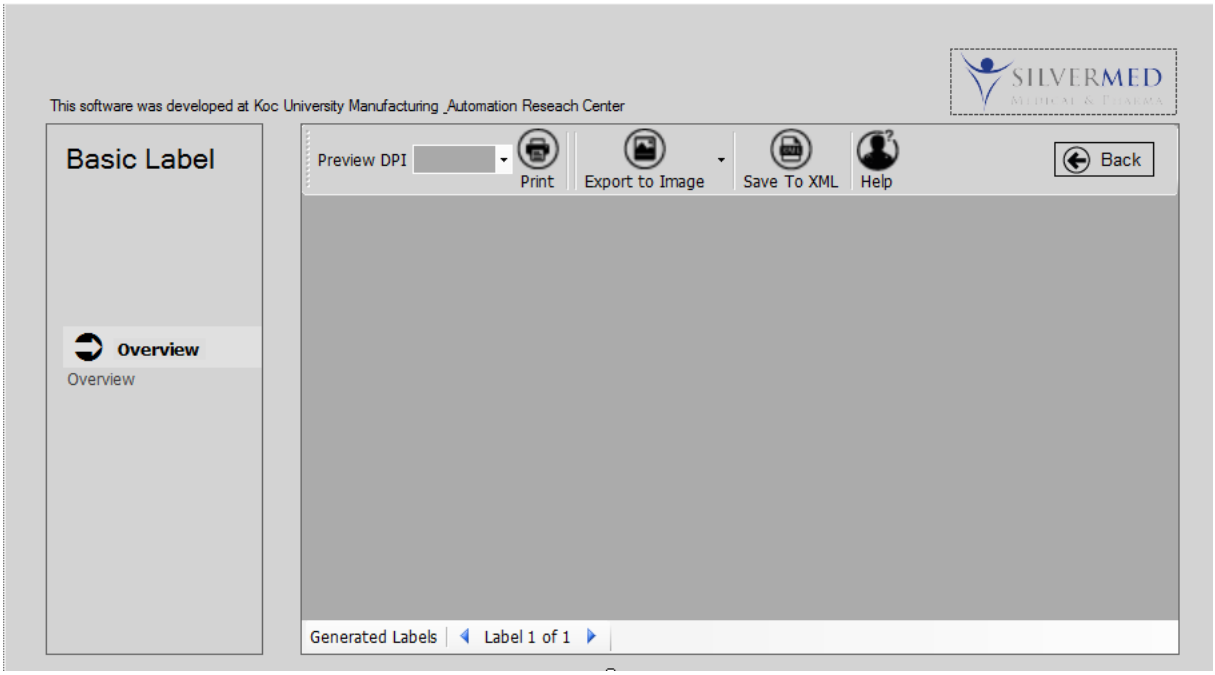

Figure 5-14: Interfaces for Printing Receipts

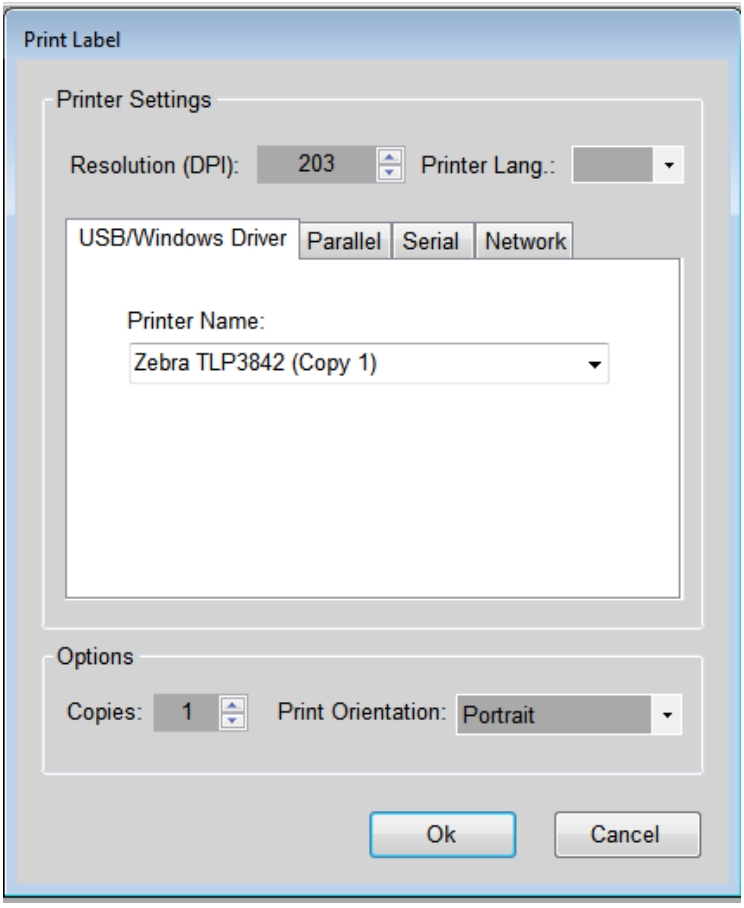

Figure 5-15: Print Setting Dialog

Each cycle of drug preparation by a specific user completes here. After printing the labels, main screen of new drug preparation shown in figure 5-12 will come on front screen again. If user wants to logout he presses “LOG OUT”, but if user wants to prepare another medicine for another patient or same patient, he/she will press “DONE”.

5.5.2.10 Verification of Used Drug

There are three labels generated from the printer after each drug dosing routine. Two of them are for prepared drug. One of them will be attached with prepared drug for patient and other will glued to the dosage delivery record register of administration. The third label is label for used source vial. Next time when a user wants to reuse this vial, scanning the barcode on third label remaining amount of drug in vial automatically appears in the field of “available amount”. But before using used drug for new drug preparation, if user wants to verify the validity of the drug, he/she can verify the drug through interface shown in figure 5-15.

Figure 5-16: Verification of Used Drug

6 INTERFACING DEVICES

6.1 Introduction

In this system, controlled dosing become possible by applications like controlled software routines, barcode medication administration and customized printed receipts. In addition to these feature, there is additional feature in existing electronic medication administration records. Presented system has an interface with camera and software routine bounds the user to first take image of the label of source drug and save it. For all these features like barcode medication administration, customized printed receipt and image medication record, this system needs following three interfacing devices.

- Printer
- Barcode Scanner
- Camera

In this chapter, section 6.1 describe barcode scanner's interface, its hardware connection, drivers and software programming for data reception, section 6.2 gives detail about hardware and software details of camera attached with the system, section 6.3 describe hardware and software details of the printer.

6.2 Barcode Scanner Interface

Barcode technology has been invented by Norman J Woodland in 1949 [28]. Thanks to him, time consuming tasks from shopping on grocery stores to verification of serious medication, all become easy to do and more reliable. Barcode of each item is a pattern of unique numbers, presented in a way shown in figure

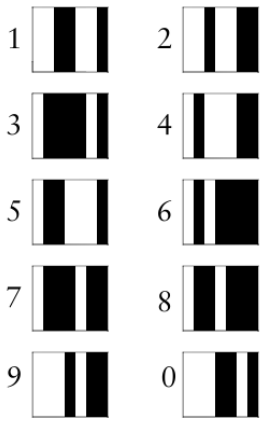

Figure 6-1: Pattern of Numbers in Barcode [29]

Barcode scanners read these black and white patterns of line and send the information to the computer as binary numbers. Computer reads these binary numbers are converting them to digital. Typical procedure of whole process proceeds in following steps [29]:

- LED or laser light shines on the barcode
- This light after striking with barcode pattern reflects back and receives by light detecting photoelectric cells.
- As white spaces reflects more light and black line reflect less, therefore scanner's photoelectric cell read "ON" for white and "OFF" for black.
- In this way, scanner interpret pattern information into binary code e.g. 010001110 and send this information to computer

For implementing feature of barcode medicine administration system, a barcode scanner has been interfaced with the system. Below is the hard ware and software detail of the interfacing.

6.2.1 Hardware Connectivity

After connecting a corded barcode scanner with the computer, one should know the suitable connectivity type of it. Corded barcode scanner can be connected to PC by following four ways:

- **USB:** Barcode scanner connects to PC by a USB port therefore when it is connects first time it is recognize as Human Interface Device in PC device Manager.
- **Keyboard Wedge:** Before USB method of connection, barcode scanner was connected by a Y-type wire, one end of wire connects with the keyboard and other to the PC.
- **RS232 Serial:** In this type of connection barcode scanner connects with a 9 or 25 pin female connector and communicate with PC via serial port. In this case scanner occupies a COM port.
- **Interface Controller:** These types of barcode scanner come with a specialized cord and have capability to work as any of the above type. Programming has been done into these devices which make them appropriate for communication with whatever they are plugged-in.

In this thesis, interface controller barcode has been used. It is connected by a USB port and default settings make it appear as a human interfacing device. But software of this thesis requires the scanner to communicate through serial port. Therefore an RS232 Serial connection has been built by going through following steps:

- Install Virtual Com Port Driver software in PC.
- Connect the barcode scanner with the USB port of PC, and ensure its presence in Human Interface Devices by going in to Device Manager.
- In barcode scanner's company manual there will be some connectivity settings. Each setting can be saved in the scanner by scanning the barcode given for each setting. Scan barcode mentioned in front of Virtual Com Port Device Settings.
- Select barcode scanner interface in Human Interface Device and right click it. Select Properties→Update driver→ Browse drivers in your computer→ Let me pick from the list of drivers→ Select installed virtual com port driver.

In this way barcode scanner will be connected with RS232 Serial connector.

6.2.2 Software Connectivity

As this application of dosing system has been developed in Window Form Application of Visual Studio, therefore to use barcode scanner with this system an interface of serial port needs to be drag from the toolbox. By right clicking the interface click on the properties. Set properties as shown in the figure

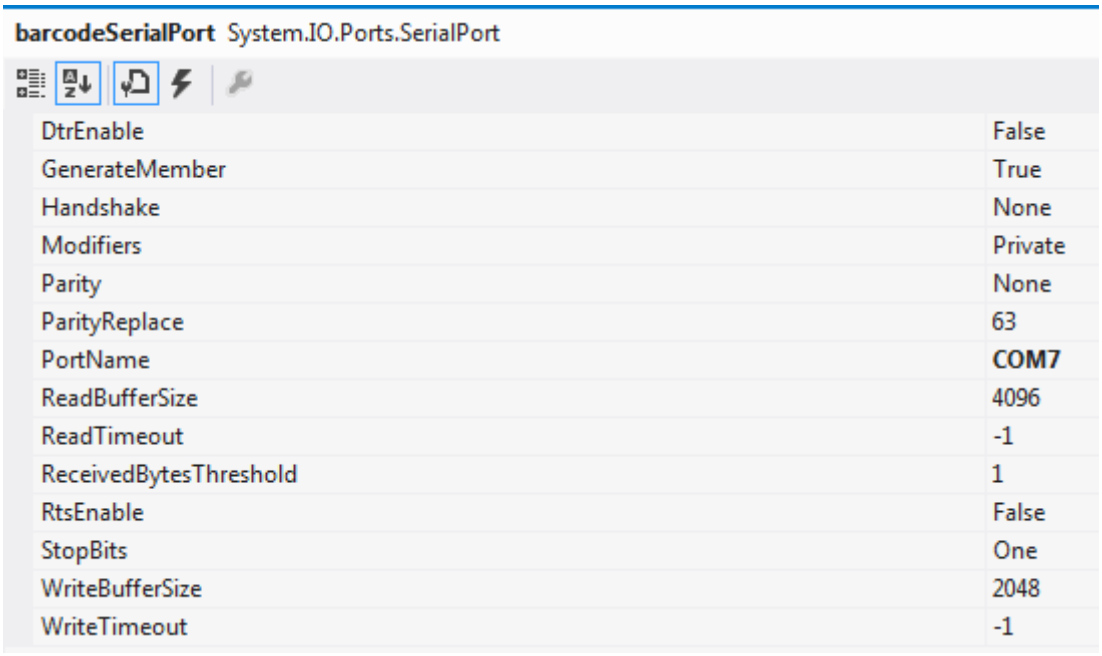

Figure 6-2: Properties of Serial Interface for Barcode

Port name must be changed according to the port occupied by virtual com port driverCamera Interface

A camera has been interfaced with the system to provide an additional characteristic to the electronic medication administration records. For each preparation software routine compels user to first take picture and then proceed further. User will take picture of source drug label and save it the system.

6.2.3 Hardware Connectivity

A high definition camera has been connected via USB port of the system. Driver of camera needs to be installed. After installing the driver of camera, camera device has been detected by computer as an imaging device. Software of the system directly gets data from this device in imaging devices shown in device manager.

6.2.4 Software connectivity

In order to access the imaging device through the software Visual Studio need a reference of respective library. That can be downloaded online. After installing the library, reference of this library should be added to the application.

6.3 Printer Interface

A printer is also interfaced with the system. Printer manufactured by zebra technologies has been used in this system for its compact design and easily available drivers and libraries. This printer uses the zebra programming language and zebra driver. Below sections contain hardware connectivity and software programming details for the printer.

6.3.1 Hardware Connectivity

Printer is attached by a USB, bi-directional interface. Printer has external power supply of 220V. Driver of this printer can be found easily from the internet provided by the manufacturers. After downloading the driver, technician should update driver of the connected USB printer.

6.3.2 Software connectivity

In this system application, an already build project of Thermal label SDK printer has been used. Changes have been done to the projects to meet system's requirements. All the information is received by printing class. In this system EPL language of zebra technologies has been used which print above mentioned information and the barcodes to print out customized receipts of the drug preparation.

7 USER GUIDE

7.1 Introduction

This chapter intended to describe guidelines for pharmacist and nurses to use this system. For each prescription user has to assemble new set of apparatus and go through software routine. This user guide provides the information and instructions needed to set up and use this system to prepare each drug prescribed by the doctor.

7.1.1 Process Overview

For compounding and dosing each drug for a patient, user needs to go through a specific routine. This routine can be divided into three parts for better explanation;

- **Pre-Compounding and Dosing Setup:** It involves preparing system's setup for compounding.
- **Compounding and Dosing Routine:** It involves user-controlled software routines for compounding and dosing.
- **Post-Compounding and Dosing Setup:** It involves preparing setup for injecting compounded drug in target vial.

7.2 Procedure

Following are the steps to follow for compounding and dosing the prescribed drug;

7.2.1 Pre-compounding and dosing setup:

1. **STEP-** Connect manifold to the syringe.
2. **STEP-** Connect syringe with clamp of the system.
3. **STEP-** Connect source vial to the vial adaptor.
4. **STEP-** Connect vial adaptor to the manifold.

7.2.2 Compounding and Dosing Software Routine:

1. **STEP-** Power-ON the system selects the language option.
2. **STEP-** Enter login ID and password. If user is not registered, he/she has to register by first clicking "register new user". And fill the form and register him/her. After that, login by user ID and password.
3. **STEP-** Next screen is the home page. This page has three option
    - **Login Patient:** If Patient is already registered, drug can be prepared for him by going through patient login.

- **Logout:** This interface is used to logout the user account.
- **Register New Patient:** This interface registers new patients to the databases.
- **Verify Drug:** This interface verify used drug.

4. **STEP-** Next step is Patient Login page. If patient is already registered user has to follow following steps;
    - User has to enter the hospital ID of patient and click OK.
    - System will display name of patient. User has to confirm patient's name.

    If patient is not already registered. Register patient in hospital database by clicking "Register new user".
5. **STEP-** In next step, detail of recent dosage displays, user has to select "New Drug Preparation" to proceed. Or user can select back to go back page.
6. **STEP-** Next is the main new drug preparation interface. Following steps should be followed;
    - User has to "START" button to start camera routine, "CAPTURE" to capture the image of source drug vial. And finally save it by pressing "SAVE".
    - User has to select a channel between 20ml syringe and 60ml Syringe, depending upon the amount of dosage.
    - Patient name has been automatically appeared on the screen. It is name of the logged in patient.
    - User has to select prescriber's name. If user cannot find prescriber name in drop down list, he/she needs to add the prescriber in system database. This can be done by clicking "ADD PRESCRIBER" button.
    - User has to put drug's detail. First of all he/she needs to scan the barcode of the drug. If name of the drug do not appear in the field of drug name, then the possibility is drug is not present in the drug database. For this possibility drop down the list of medicines. If user cannot find name of medicine it means that he/she needs to register the medicine before use. If name is present but scanning barcode do not make it appear in the field then do troubleshooting step (refer to section 8.1.2)
    - In order to register the medicine user need to press "UPDATE DRUG LIBRARY" button.
    - If user wants to update a drug library by importing an authorized drug list in excel format, he/she can import drug list by pressing "IMPORT DRUG LIBRARY".

- After scanning the barcode, user need to mention available drug in the source vial of drug. Available amount must be given in unit of milliliter.
- User needs to mention needed amount of source vial drug for the preparation of new drug. User can also put prescribed mass of the drug by mentioning the concentration of drug. After that user presses “CALCULATE” button to fill the field of amount in milliliters.
- After mentioning name, available amount and required amount user needs to mention the speed of drug preparation. Speed should be selected depending upon the viscosity of drug.
- After mentioning the Prescriber’s information and drug’s information, user presses button “START” to suck the drug from the source container/vial.
- After progress bar shows 100% complete process, button interface “INJECT” will appear.
- Connect straight spike adaptor and flexible bag
- Connect flexible bag to manifold (syringe adaptor on manifold)
- User has to press INJECT button, plunger inject drug in to target container(flexible bag)
- After injection, user has to press PRINT SUMMARY. In order to print three receipts.
- Detach flexible bag and straight spike adaptor from manifold and glue label on it
- Detach vial with vial adaptor from manifold, then glue label on it (if it is empty then discard)
- Detach syringe and manifold together from machine. Then discard.

7. **STEP-** If user wants to logout he presses “LOG OUT”, but if user wants to prepare another medicine for another patient or same patient, he/she will press “DONE”.

8 TROUBLESHOOTING

8.1 Introduction

This chapter provides the procedure for troubleshooting various hardware or software problems that may come while working on the system.

In this chapter, section 8.2 give details for troubleshooting that can be done by user of this system and section 8.3 provide information for the troubleshooting that can only be done by technicians.

8.2 Troubleshooting by User

8.2.1 Camera Screen Not Appears When User Click Start:

- **Reason:** Camera is interfaced as imaging devices. Sometimes imaging device is not ready to use then button START on clicking show an error.
- **Troubleshooting:** Click OK on error message and click START button again.

8.2.2 Drug Name Do not Appear in Textbox When Scan Barcode:

- **Reason1:** One reason can be this that drug has not been registered in drug database.
- **Troubleshooting:** Drop down the drug name list and confirm the presence of drug. If drug is not present, first register the drug.
- **Reason2:** Second reason can be inactivation of textbox.
- **Troubleshooting:** Click the text box and scan the barcode again, it will be scanned.

8.2.3 Emergency Stop Button:

If user needs to press the emergency stop button due to any reason, to reset the system and start its working precisely, he/she needs to reset the system. For this user needs to press button RESET.

8.2.4 Serial Port is missing:

Reason: This error message can come along if any of the barcode scanner USB connection or electronic interface device USB connection is loss or disconnected.

Troubleshooting: This error can be eliminated by first connection the device precisely. Then click OK on error.

8.2.5 Rebooting Printer after Changing Reel:

Reasons: After each reel change printer's alignment can be disturbed. Therefore after a new reel has been putter in printer, Printer needs to be rebooted.

Troubleshooting: Rebooting of printer can be done by pressing power-OFF button (on the back of printer). Now press button on top of the printer, keep it pressed and Power-ON button. Light of button in the front of printer will be red for some time. Release the top button. Now printer will automatically reboot itself. In end of rebooting, follow instruction on the receipt to click top button. By clicking top button printer will come out of the dump and completes its setting.

8.3 Troubleshooting by Technicians

8.3.1 Troubleshooting for Software

Troubleshooting of software can be done by technician, for that technician needs to access by technician login. On the first screen of user login, user can click button of TECHNICAL ACCESS. When he/she clicks, a new screen appears that has been shown in figure 8-1:

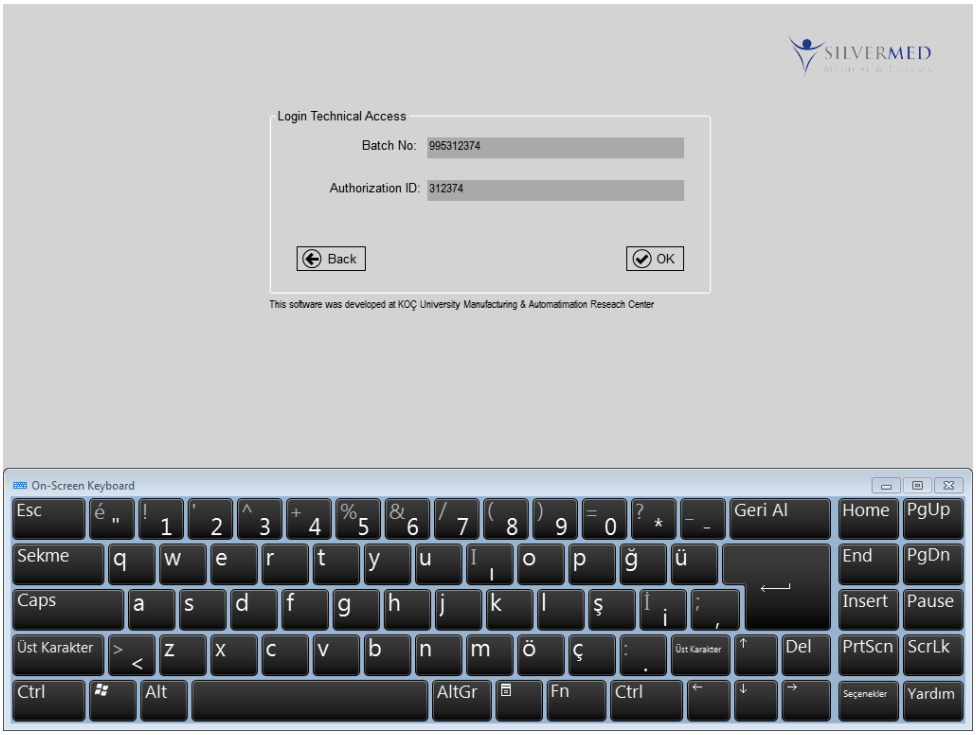

Figure 8-1: Technical Access Login

There will be a unique batch number and corresponding authorization ID. After putting this information technician can get exist to three two options;

- Access the machine history
- Exit the application

Technician can exit the application to troubleshoot any issue in programming that cannot be solved by user during routine. In figure 8-2

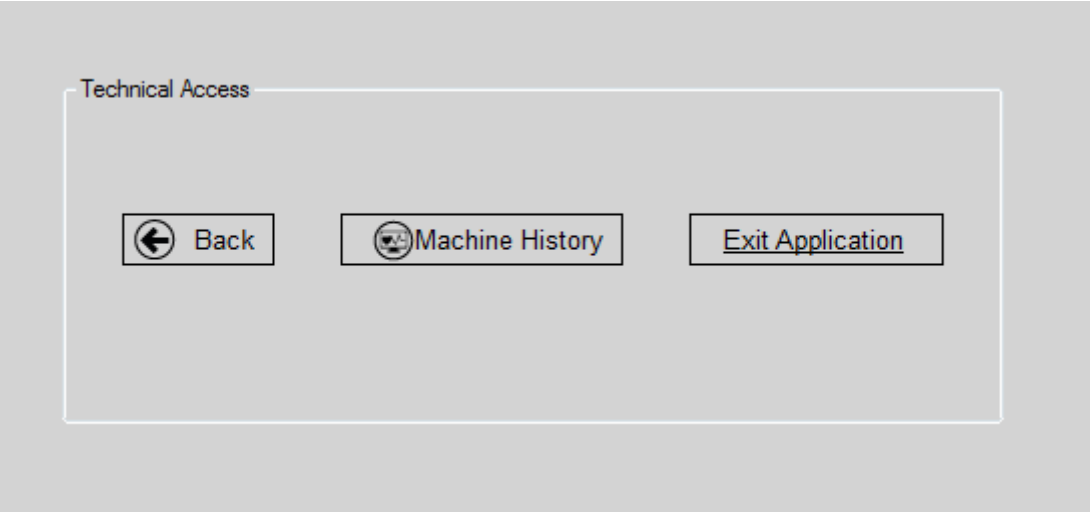

Figure 8-2: Technician Access

8.3.2 Troubleshooting of Hardware

Main hardware problem can be due to motor drives. However the drives used in the system have LED display of alarms on each problem caused by any reason. In Appendix C there are some of the errors that can solve by technician by the methods given.

9 CONCLUSION

This study demonstrates the capabilities of high-precision compounding and controlled dosing system to deal with the most frequent problems related to compounding and dosing of occupational hazardous drugs. This system automates the workflow for a sterile, safe and accurate compounding process. Closed transfer devices used in this system preclude hazardous effects of antineoplastic agents and cytostatic drugs. Controlled dosing routine of the system helps the pharmacists and nurses to avoid errors like wrong volume of drugs and delivery of drug to wrong patient by constantly taking account of patient history stored in the system. Access of the irrelevant users has been prohibited by providing login account to the system application. Login access, patient account and prescriber's detail, provided with each drug dosing process, make the system capable to efficiently deal with legal consequences.

For efficient and error-free compounding, system uses barcode medication administration system. Authentic drug library can be updated into the database which avoids usage of any inferior quality or unauthorized drug.

Moreover, feature of electronic medication administration record (eMAR) has been added in to the system. eMAR helps the administration to follow the history of each patient and keep record of: 1) date and time of dosage delivery, 2) name of the pharmacist/nurse who prepared the drug, 3) detail of the prescriber/doctor, 4) name and barcode of the drug used for drug compounding, 5) speed of preparation.

For each compounding dosing process, the automated routine of high-precision compounding and controlled dosing system oblige the pharmacist/nurse to take an image of the used drug vial as a further measure of evidence.

This study gives details of accuracy tests performed to analyze the performance of high-precision compounding and controlled dosing system. Error below 1ml for each sample prepared by both channels proves high precision of the system.

User-controlled automation, high accuracy, needle-free closed transfer assembly and cost efficiency make this system highly effective. Database for authorized medicine, barcode medicine administration, electronic medical administration records and limited access to user and patient account are new milestones in existing technologies of compounding and dosing systems.

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APPENDIX A

MOTOR DRIVES ALARMS LIST

Display	Alarm Name	Alarm Description	Corresponding DO	Servo Status
AL001	Over current	The current of the main circuit is 1.5 times more than the instantaneous current of the motor.	ALM	Servo Off
AL002	Over voltage	The voltage of the main circuit is higher than the standard voltage.	ALM	Servo Off
AL003	Under voltage	The voltage of the main circuit is lower than the standard voltage.	WARN	Servo Off
AL004	Motor Combination Error	The drive corresponds to the wrong motor.	ALM	Servo Off
AL005	Regeneration Error	Regeneration control is in error.	ALM	Servo Off
AL006	Overload	The motor and the drive is overload.	ALM	Servo Off
AL007	Over speed	The control speed of the motor exceeds the normal speed.	ALM	Servo Off
AL008	Abnormal Pulse Command	The input frequency of the pulse command is over the allowable value of the hardware interface.	ALM	Servo Off
AL009	Excessive Deviation of Position Command	The deviation of position command exceeds the allowable setting value.	ALM	Servo Off
AL011	Encoder Error	The encoder produces abnormal pulse.	ALM	Servo Off
AL012	Adjustment Error	When executing electrical adjustment, the adjusted value exceeds the allowable value.	ALM	Servo Off
AL013	Emergency Stop	Press the emergency stop button.	WARN	Servo Off
AL014	Reverse Limit Error	Activate the reverse limit switch.	WARN	Servo On
AL015	Forward Limit Error	Activate the forward limit switch.	WARN	Servo On

Display	Alarm Name	Alarm Description	Corresponding DO	Servo Status
AL016	IGBT Overheat	The temperature of IGBT is over high	ALM	Servo Off
AL017	Abnormal EEPROM	It is in error when DSP accesses EEPROM.	ALM	Servo Off
AL018	Abnormal signal output	The encoder output exceeds the rated output frequency.	ALM	Servo Off
AL019	Serial Communication Error	RS-232/485 communication is in error	ALM	Servo Off
AL020	Serial Communication Time Out	RS-232/485 communication time out	WARN	Servo On
AL022	Main Circuit Power Lack Phase	Only one single phase is inputted in the main circuit power.	WARN	Servo Off
AL023	Early Warning for Overload	Early Warning for Overload	WARN	Servo On
AL024	Encoder initial magnetic field error	The magnetic field of the encoder U, V, W signal is in error.	ALM	Servo Off
AL025	The Internal of the Encoder is in Error	The internal memory of the encoder and the internal counter are in error.	ALM	Servo Off
AL026	Unreliable internal data of the encoder	The error of the internal data has been detected for three times continuously.	ALM	Servo Off
AL027	The Internal of the Encoder is in Error	The internal reset of the encoder is in error	ALM	Servo Off
AL028	The Internal of the Encoder is in Error	The encoder, U, V, W signals are in error	ALM	Servo Off
AL029	The Internal of the Encoder is in Error	Internal address of the encoder is in error	ALM	Servo Off
AL030	Motor Crash Error	The motor crashes the equipment, reaches the torque of P1-57 and exceeds the time set by P1-58.	ALM	Servo Off
AL031	Incorrect wiring of the motor power line U, V, W, GND	Incorrect wiring of the motor power line U, V, W, GND or the connection between both is breakdown.	ALM	Servo Off

Display	Alarm Name	Alarm Description	Corresponding DO	Servo Status
AL035	Encoder temperature exceeds the protective range	Encoder temperature exceeds the protective range	ALM	Servo Off
AL048	Excessive encoder output error	The encoder output errors or the output pulse exceeds hardware tolerance.	ALM	Servo Off
AL067	Encoder temperature warning	Encoder temperature exceeds the warning level. (But it is still within the protective range.)	ALM	Servo Off
AL083	Servo drive outputs excessive current	When the output current from servo drive exceeds the setting level, ALE083 will be triggered to protect IGBT. This could avoid IGBT to be burned out because of the excessive current.	ALM	Servo Off
AL085	Regeneration error	Regeneration control is in error.	ALM	Servo Off
AL099	DSP Firmware Upgrade	EEPROM has not been reset after upgrading the firmware. The fault can be cleared when firstly set P2-08 to 30. Then set P2-08 to 28. And re-power on the drive.	WARN	Servo On
AL555	System Failure	DSP processing error	N/A	Do not Switch
AL880	System Failure	DSP processing error	N/A	Do not Switch