A small molecule drug screening identifies colistin sulfate as an enhancer of Natural Killer cell cytotoxicity.

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Abstract:

Because of their crucial role in tumor immunity, NK cells have quickly become a prime target for immunotherapies, with adoptive transfer of NK cells and the use of NK cell engagers quickly moving to clinical stage. On the other hand, only few studies have focused on small molecule drugs capable of unleashing NK cell against cancer. In this context, repurposing small molecule is an attractive strategy to identify new immunotherapies from already approved drugs. Here, we screened 1,200 FDA-approved drugs from the Prestwick Chemical Library, to identify compounds that increase NK cell cytotoxic potential. Using a high-throughput luciferase-release cytotoxicity assay, we found that the antibiotic colistin sulfate increased cytotoxicity of human NK cells towards cancer cells. The effect of colistin was short lived and was not observed when NK cells were pretreated with the drug, showing how NK cell activity was potentiated only when the compound was present at the time of recognition of cancer cells. Further studies are needed to uncover the mechanism of action and the pre-clinical efficacy of colistin sulfate in mouse cancer models.

Keywords:

NK cells, immunotherapy, functional screen, drug repurposing
**Introduction**

Seminal studies from the 1990s and early 2000s highlighted the importance of the immune system in tumor biology through processes such as immunosurveillance and immunoeediting\(^1\), which in turn led to the most recent advances in cancer therapeutics: immunotherapies. Cancer immunotherapy is an encompassing term referring to therapeutic strategies that target components of the immune system to enhance clearance of the malignant cells. Various categories of immunotherapies exist\(^2\) and, encouragingly, some became first-line treatments in some cancer types\(^3,4\). As the field of immunotherapy continues to develop, we have gained a better understanding of how immune cells contribute to immunotherapy efficacy, for instance Natural Killer (NK) cells. NK cells are innate lymphoid cells that play a crucial role in tumor surveillance and clearance\(^5\). The importance of NK cells in immunosurveillance is appreciated from the observation that mice without functional NK cells show impaired tumor control\(^6,7\) and that patients with defective or decreased frequency of NK cells are at greater risk of developing malignancies, specifically virally induced cancers\(^8,9\). Recently, a thorough systematic review and meta-analysis encompassing 15 solid cancer types found that NK cell infiltration in solid tumors was associated with improved overall survival\(^10\), whereas lower low frequency of circulating or tumor-infiltrating NK cells or NK cells that display impaired function are associated with worse prognosis in several cancer types\(^11-14\). NK cells can either be administered for adoptive cell therapy or can be directly targeted to enhance their anti-tumor activity\(^5\). Within the second category, small molecule drugs have been surprisingly overlooked, despite evidence that small molecules can potentiate NK anti-cancer functions\(^15,16\). In addition to enhancing cytotoxicity, small molecules can also be used to promote proliferation and maturation in expansion protocols for NK cells that are used for adoptive cell therapies\(^15\). Small molecule immunotherapies are advantageous as they are orally...
bioavailable, usually cost less than biological immunotherapies, can target both extracellular and intracellular components and have a greater ability to penetrate through physiological barriers\cite{17}. However, from small molecule identification to development of a lead drug compound, the clinical drug pipeline can take years if not decades before the drug sees use in the clinic. For this reason, drug repurposing is an attractive alternative that identifies new indications for previously approved drugs. Repurposed drugs already have a safety and efficacy profile associated with them which makes this a favorable route. Several studies have conducted high-throughput drug screenings to identify drugs that modulate NK cell activity. These studies utilized commercially available libraries containing repurposed drugs\cite{18-20} or natural compound libraries\cite{21,22} and have identified small molecules that were not previously known to modulate NK cell activity. Here, we screened the Prestwick Chemical Library for compounds capable of enhancing cytotoxicity of human NK cells towards leukemia target cells and identified the antibiotic colistin sulfate as an enhancer of NK cell cytotoxicity.

**Materials and Methods.**

**Cell culture**

All cell lines were cultured in a humidified incubator at 37°C and 5% CO$_2$ in media supplemented with 100 U/ml penicillin (Gibco, CA), 100 µg/ml streptomycin (Gibco), 10 g/ml gentamycin sulfate (Gibco), 20 mM HEPES (Fisher, ON). NK92 cells were cultured in RMPI-1640 containing 10% fetal bovine serum (FBS) (Gibco). K562-NL cells were cultured in RMPI-1640 containing 5% FBS. A375-NL cells and 786O-NL cells were cultured in DMEM (Corning, VA) containing 10% FBS.
Reagents and drugs

Preparation of coelenterazine substrate: 500 μg of coelenterazine substrate (CTZ) (Gold Biotechnology, MO) was reconstituted in 610 μL of 100% ethanol and 6.2 μL of 12 N hydrochloric acid. The reconstituted substrate was protected from light and stored at -80°C until use. Prior to measuring luciferase activity, the reconstituted CTZ was mixed with 1X salt buffer (45 mM EDTA, 30 mM sodium pyrophosphate, 1.425 M NaCl) at a 1:200 dilution (5 μL CTZ per 1 mL salt buffer).

The Prestwick Chemical Library (https://www.prestwickchemical.com) was kindly provided by Dr. Diallo.

Preparation of candidate drugs: colistin sulfate salt (Sigma-Aldrich, MO), nicotinamide (Sigma-Aldrich), monensin sodium salt (Sigma-Aldrich), zafirlukast (Sigma-Aldrich), tizanidine hydrochloride (Sigma-Aldrich), closantel (Sigma-Aldrich), benazepril hydrochloride (Sigma-Aldrich), and diflorasone diacetate (Sigma-Aldrich) were prepared at a master stock concentration of 1 mM in 100% DMSO, with exception of colistin sulfate salt which was dissolved in water. A working stock concentration was prepared for all candidate drugs of 100 μM in PBS with a final DMSO concentration of 10%. All candidate drugs were stored at -20°C until use.

Fluorochrome-conjugated antibodies, all from BD Biosciences, CA: AF647-CD3 (Clone UCHT-1), APC-R700-CD4 (Clone RPA-T4), BV786-CD8 (Clone RPA-T8), PE-CD56 (Clone B159), BV711-CD16 (Clone 3G8), BV650-CD19 (Clone SJ25-C1) and PerCP-Cy5.5-CD14 (Clone MφP9).
**Generation of cell lines**

To generate K562, A375 and 78O cells expressing nanoluciferase, lentiviral particles were produced by co-transfecting 293T cells with a lentiviral plasmid encoding nano luciferase plenti-NL (a gift from Dr. Wanker through Addgene; http://n2t.net/addgene:113450; RRID:Addgene #113450), packaging plasmids pCMV-dR8.2dvpr (a gift from Dr. Weinberg through Addgene; http://n2t.net/addgene:8455; RRID:Addgene #8455) and pCMV-VSV-G (a gift from Dr. Weinberg through Addgene; http://n2t.net/addgene:8454; RRID:Addgene_8454), following Lipofectamine 3000 transfection instructions for a 10 cm dish (Invitrogen, CA). 72 hours following the transfection, supernatant containing lentiviral particles was collected and used to transduce K562, A375 and 786O-NL cells by spin-infection (500 g for 2 hours at 37˚C) with 8 μg/mL polybrene (Sigma-Aldrich). Four days post-transduction, nano luciferase expression was confirmed by using the Nano-glo luciferase assay system (Promega, WI). After nano luciferase expression was confirmed, single cells from the transduced cell populations were sorted into five 96-well plates using the MoFlow XDP Cell Sorter (Beckman Coulter, CA). After several weeks of culture, wells with cell growth were tested for luciferase expression. Selected clones were mixed at an equal ratio to make a polyclonal population.

**Luciferase release-based cytotoxicity assay**

NK92 cells were co-cultured with target cells expressing NL in triplicate at various E:T (effector:target) ratios in RPMI 5% FBS in 96-well V bottom plates (Sarstedt, QC) for 5 hours at 37˚C. After the incubation, 50 μL of supernatant from each well was transferred to round-bottom black 96-well plates (Corning, ME). Depending on the experiment, either 25 μL of Nano-glo substrate or CTZ substrate was added to each well and the Biotek Synergy Mx plate reader (Biotek,
VT) was used to measure luminescence. Percentage (\%) specific lysis was calculated using the following equation (Equation 1), where experimental release are the raw luminescence values from NK92+target cells, spontaneous release are the raw luminescence values from the target cells in absence of effector cells, and maximal release are the raw luminescent values from target cells treated with 30 μg/mL of digitonin (Sigma-Aldrich).

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\% \text{ specific lysis} = \frac{(\text{experimental release} - \text{spontaneous release})}{(\text{maximal release} - \text{spontaneous release})} \times 100 \quad \text{(Equation 1)}
\]

*Flow cytometry-based cytotoxicity assays*

Flow cytometry-based cytotoxicity assay was performed as described before\textsuperscript{23}. Briefly, NK92 cells were co-cultured with CFSE-labelled targets cells in triplicate at various E:T ratios with 10,000 target cells per well in RPMI 5% FBS in 96-well V bottom plate (Sarstedt) for 5 hours at 37°C. Cells were then stained with Zombie NIR™ Fixable Viability Kit (Biolegend, CA). Prior to acquisition, APC counting beads (Spherotech, IL) were added. Samples were acquired using the HTS function of the LSR Fortessa (BD Biosciences). Percentage specific lysis was calculated using Equation 1, where experimental release is the ratio of beads to live target cells from NK92+target cell wells, spontaneous release is the ratio of beads to live target cells from the target cells in absence of effector cells wells, and for maximal release, the value 0 was used as we would expect there to be no live cells.

*Screening of the Prestwick Chemical Library and plate configuration*

The Prestwick Chemical Library, which contains 1,200 regulatory-approved drugs, was screened to identify compounds capable of enhancing NK92 cytotoxicity. K562-NL cells alone or a
co-culture of NK92+K562-NL cells at a E:T ratio of 1 were treated with 10 μM of each drug for 5-hours at 37°C. Each compound was evaluated in singlet over 2 independent experiments.

The Prestwick Chemical Library’s 15 stock plates were stored at -20°C in 10% DMSO at a concentration of 100 μM in deep well plates (Axygen, Tamaulipas, Mexico), with compounds only in columns 2-11. On the day of the screen, the stock plates were thawed, and the Bravo Automated Liquid Handling Platform (Agilent, CA) was used to dispense 10 μL of each drug (final drug concentration of 10 μM) to columns 2-11 to a total of thirty 96-well V-bottom assay plates (Sarstedt). For the 15 assay plates containing K562-NL cells alone, 45 μL of K562-NL cells plus 45 μL of media was dispensed to all columns for a final assay volume of 100 μL. For the 15 assay plates containing K562-NL+NK92 cells, 45 uL of K562-NL was dispensed to all columns and 45 μL of NK92 cells was dispensed from column 1-11 for a final assay volume of 100 μL. Controls were dispensed in column 1 and 12 for each assay plate. For all 30 assay plates, 10 μL of 10% DMSO was dispensed to column 1 (final DMSO concentration of 1%). For the 15 assay plates containing K562-NL cells alone, 10 μL of 300 μg/mL of digitonin was dispensed to column 12 (final concentration of 30 μg/mL) as a maximal release control. For the 15 assay plates containing K562-NL+NK92 cells, NK92 and K562-NL cells were dispensed at a 9:1 E:T ratio in column 12 as a positive control for NK92 cytotoxicity. Negative controls in column 1 were K562-NL+DMSO (K562-NL alone plates) and 1:1 E:T+DMSO (NK92+K562-NL plates). Plate layouts is depicted in Supplementary Fig. 1.
After the incubation, 50 μL of supernatant from each assay plate was transferred to round-bottom black 96-well plates (Corning, ME) using the Bravo Automated Liquid Handling Platform. Biotek plate reader was used to dispense 25 μL of CTZ to each well and measure luminescence.

Z’ factor, fold-change and normalization analysis
Raw luminescence values from the screenings were used to calculate Z’-factor and luminescent fold-change. To evaluate the overall screening assay stability, Z’ factor was calculated for each assay plate using the negative (column 1: DMSO) and positive (column 12: 9:1 E:T or digitonin) control values in each plate. Equation 2 was used to calculate Z’ factor, where SD+ represents the standard deviation of the positive control, SD− represent the standard deviation of the negative control, m+ represents the mean of the positive control and m− represents the mean of the negative control.

\[
Z' = 1 - \frac{3SD^+ + 3SD^-}{|m^+ - m^-|} \quad \text{(Equation 2)}
\]

To identify compounds capable of enhancing NK92 cytotoxicity, the luminescent fold-change over DMSO control was calculated for all compounds in the E:T=1 condition and K562-NL alone condition. Compounds that had a fold-change ≥1.3 were considered drug hits. Drugs were excluded if the fold-change was ≥1.3 in the K562-NL alone treated with drugs condition. Fold-change for each plate was calculated by using the controls on individual plates.
Dose-response experiments

K562-NL cells alone or NK92 and K562-NL cells mixed at a 1:1 and 3:1 E:T ratio were treated with either 0, 1, 5, 10 and 20 μM of drug candidates for 5 hours at 37°C. Luciferase activity was measured as previously described.

Colistin sulfate pre-treatment

NK92 or K562-NL cells alone were treated for either 24 hours or 1 hour with 10 μM of colistin sulfate. Prior to mixing the cells together, the drug was washed out. Pre-treated NK92 cells were mixed with untreated K562-NL cells, and pre-treated K562-NL cells were mixed with untreated NK92 cells. A condition where drug treatment was present during the 5-hour incubation was also included. Luciferase activity was measured as previously described.

Human PBMC isolation

Human blood samples were obtained from healthy donors using the Perioperative Human Blood and Tissue Specimen Collection Program protocol approved by The Ottawa Health Science Network Research Ethics Board (OHSN - REB 2011884-01H). PBMCs were isolated from peripheral blood of healthy donors by Ficoll (GE Healthcare, Sweden) gradient centrifugation at 19°C. Cells were resuspended in CryoStor® CS10 and cryopreservation of cells was followed according to the manufacturer’s instructions (BioLife Solutions, WA).
Human NK cell cytotoxicity assays with colistin treatment

Previously frozen human PBMCs from healthy donors were thawed according to CryoStor® CS10 thawing cells protocol (BioLife Solutions), afterwards, PBMCs were kept overnight at 4°C. NK cells were isolated from PBMCs using EasySep™ Human NK Cell Isolation Kit (Stemcell Technologies, BC). NK cells were co-cultured with K562-NL cells at different E:T ratios and treated with 10 μM of colistin for 5 hours at 37°C. Luciferase activity was measured as previously described.

Statistical analysis

Statistical analyses conducted included unpaired two-tailed Student’s t test, one or two-way ANOVA with either Dunnett’s, Sidak, Tukey’s or Bonferroni’s multiple comparison test, as described in the figure captions. Statistical significance was achieved when the p value was ≤0.05. GraphPad Prism 9 was used for statistical analyses. For flow cytometry experiments, FlowJo V.10.7.1 was used for analysis.

Results

Generation of K562-NL and validation of a luciferase release-based killing assay

Traditional methods to assess NK cell cytotoxicity such as chromium-release or flow cytometry-based assays are difficult to scale up for a high-throughput use. Luciferase release-based killing assays have proven useful to perform drug screenings24, and a luciferase released-based screen was employed in a previous NK cell drug screening18. To generate target cells suitable for a luciferase release-based NK cell killing assay, we transduced the myeloid leukemia cell line K562 with a lentiviral plasmid encoding nano luciferase (NL). Expression of NL was assessed on
transduced K562 cells by exposing cellular lysates to the substrate: no signal was observed from the lysate of control cells, whereas a robust signal was detected from the lysate of transduced K562 cells (Sup. Fig. 2A). Once we verified NL expression on K562 cells, we employed K562-NL as targets in a luciferase release-based killing assays using the NK cell line NK92 as effectors. Consistent with what expected in cytotoxicity assays, the presence of effector cells increased the luminescence signal in a dose-dependent manner, indicating that the target cells were effectively killed, whereas the luminescence signal observed with target cells alone was similar to that of the media only (Fig. 1A).

Next, we sought to obtain a polyclonal population of K562 cells expressing NL from the transduced population, which likely contained cells which were not transduced. Therefore, we sorted single cells into five 96-well plates and tested wells where cell growth was observed for luciferase expression. K562 clones expressing NL were then tested in cytotoxicity assay vis-à-vis with the unsorted K562-NL population (Sup Fig. 2B). Clones that were killed by NK92 cells similarly to the K562 bulk population were selected and mixed at an equal ratio to make a polyclonal population of K562-NL cells, which was then used in all subsequent experiments.

Optimization of the conditions for a high-throughput luciferase release-based cytotoxicity assay

For these first experiments, to test NL activity, we used furimazine (FMZ), the optimized substrate for NL. However, using furimazine in a high-throughput setting is not feasible due to the high cost of the substrate. Therefore, we explored if the less expensive substrate coelenterazine (CTZ), widely used for Renilla and Gaussia luciferase, could be used as an alternative. After conducting a luciferase release-based cytotoxicity assay, we used either FMZ or CTZ to assess NL activity.
side-by-side. Luminescent signal was detected with both substrates, although the magnitude of luminescence was higher using FMZ (Fig. 1B). However, the dynamic range between targets only and the E:T ratio of 1 was comparable between the two substrates, and CTZ maintained the same dose-response observed using FMZ, indicating that CTZ could effectively replace FMZ as a substrate for these experiments.

Next, we set to determine the ideal E:T ratio to use for the drug screening. We conducted several luciferase release-based cytotoxicity assays that included a range of E:T ratios and chose to use a E:T ratio of 1 as this ratio shows minimal killing but still has detectable luminescence above K562-NL target cells alone and there is large dynamic range between the 1 and 81 ratios, an E:T ratio that shows saturation in killing (Fig. 1C).

As a positive control for the screen, we decided to use the mild detergent digitonin, as we found it able to effectively lyse targets cells without compromising NL activity (Fig. 1D).

For these set-up experiments, the supernatant from the luciferase-release cytotoxicity assay was collected and transferred to a new plate after a centrifugation step, which would be hardly feasible in high-throughput conditions. Our concern was that by skipping the centrifugation step prior to collecting the supernatant, we would capture live target cells that would lyse after addition of the substrate, resulting in similar luminescence detection between target cells alone and target+effector cells. Therefore, to determine if this step was required, we tested the difference between directly collecting the assay’s supernatant at the end of the cytotoxicity assay with or without a centrifugation step. To our advantage, the difference between the target cells alone and
target-effector cells condition was still retained without the centrifugation step (Fig. 1E). Based on these results, we deemed that a centrifugation step prior to supernatant collection was unnecessary and decided to proceed with directly collecting the assay supernatant for the drug screening.

Finally, to optimize the high-throughput drug screening workflow, we needed to estimate if leaving the effector or target cells at room temperature for an extended amount of time before they were seeded would affect the results as, logistically, we could not keep cells in their cell culture conditions (humidified incubator, 37°C, 5% CO₂) when seeding the drug screening assay plates. We simulated drug screen plating conditions by incubating NK92 and K562-NL cells separately at room temperature for 0, 60, 120, 180, and 240 minutes before the cells were seeded into assay plates. We observed that leaving the cells at room temperature more than 120 minutes before being seeded into assay plates gradually but substantially decreased NK92 cytotoxicity (Fig. 1F). We also observed a slight increase in spontaneous lysis in the K562-NL alone condition as time progressed, shown by the increase in luminescence detection at the last two time points (Fig. 1F). Based on these results, we concluded that cells had to be seeded within 1-hour to maintain the dynamic range between the experimental and control conditions.

**Screening of the Prestwick Chemical Library to identify enhancers of NK cell cytotoxicity**

To identify compounds that enhanced NK cell cytotoxicity, we employed the Prestwick Chemical Library. K562-NL cells alone or NK92+K562-NL cells mixed at a E:T ratio of 1 were treated with 10 μM of each drug for 5 hours at 37°C (Fig. 2A). Each compound was evaluated in singlet over 2 biological replicates. To identify compounds that increased NK92 cytotoxicity, the luminescent
values of all wells containing drugs were compared to the DMSO control wells from the same plate and this difference was quantified as fold-change over DMSO control (Fig. 2B). Fold-change values for all compounds and the list of excluded compounds are listed in Supplemental Tables 1 and 2.

Compounds with a fold-change $\geq 1.3$ were considered to have increased NK cell cytotoxicity. We identified 87 drugs that had a fold-change $\geq 1.3$ from the first screening of the Prestwick Chemical Library and 119 drugs that had a fold-change $\geq 1.3$ from the second screening. From this list, only Alexidine dihydrochloride proved to be toxic for target cells even in absence of effectors, and was therefore not further considered. 14 compounds from the total drugs identified had a fold-change $\geq 1.3$ on both screening days (Table 1). From these 14 drugs, 8 candidate drugs were selected for follow-up experiments. Drugs with higher fold-change were prioritized and drugs that were no longer in use, not available in the North American market or were already known to be enhancers of NK cytotoxicity were excluded. The 8 candidate drugs and associated fold-change were colistin sulfate salt (2.02), nicotinamide (1.85), monensin sodium salt (1.62), zafirlukast (1.54), tizanidine hydrochloride (1.42), closantel (1.41), benazepril hydrochloride (1.40), and diflorsone diacetate (1.40) (Table 1).

To evaluate the overall screening assay stability, $Z'$ factor was calculated for each assay plate from the screening of the Prestwick Chemical Library. The screening assay had an average $Z'$ factor of 0.72 for K562-NL alone plates treated with drugs and 0.44 for the NK92 + K562-NL (E:T of 1) plates treated with drugs. A $Z'$ factor close to 0.5 is considered fair and $Z'$ factor 0.5-1 is considered
good. Z'-factor for each individual plate can be found in Supplementary Table 3. Z'-factor analysis suggests that the overall quality of the drug screening was fair.

| Drug                          | Fold-change | Drug class                 |
|-------------------------------|-------------|----------------------------|
| 1 Colistin sulfate salt<sup>a,b</sup> | 2.02        | antibiotic                 |
| 2 Nicotinamide<sup>a</sup>    | 1.85        | vitamin B3                 |
| 3 Monensin sodium salt<sup>a</sup> | 1.62        | antibiotic                 |
| 4 Butirosin disulfate salt    | 1.60        | aminoglycoside antibiotic  |
| 5 Zafirlukast<sup>a</sup>     | 1.54        | anti-asthmatic             |
| 6 Amphotericin B              | 1.50        | antifungal                 |
| 7 Argatroban                  | 1.46        | anti-coagulant             |
| 8 Dimethisoquin hydrochloride | 1.45        | anesthetic                 |
| 9 Tizanidine hydrochloride<sup>a</sup> | 1.42    | adrenergic agonist         |
| 10 Closantel<sup>a</sup>      | 1.41        | anti-parasitic             |
| 11 Benazepril hydrochloride<sup>a</sup> | 1.40    | ACE inhibitor              |
| 12 Diflorasone diacetate<sup>a</sup> | 1.40    | topical steroid            |
| 13 Butoconazole nitrate       | 1.38        | anti-fungal                |
| 14 Etretinate                 | 1.34        | retinoid                   |

Table 1. Compounds identified as enhancers of NK92 cytotoxicity from screening the Prestwick Chemical Library. Listed drugs had a luminescent fold-change ≥ 1.3 on both screening days. Drug class for each compound is listed. "Candidate drugs that were selected for further investigation. "Fold-change of single screening.
Validation of candidate drugs

Initial validation of the 8 candidate drugs was conducted by performing cytotoxicity assays following the drug screening experimental conditions (E:T ratio of 1 and drug concentration of 10 µM). Of the eight drugs we tested, only colistin sulfate salt (herein colistin) increased NK cell cytotoxicity (Fig. 3A), whereas the other 7 drugs did not change, or even reduced, the ability of NK cells to kill target cells (Fig. 3B-H).

Validation was expanded over two E:T ratio (1 and 3) and over a wider range of drug concentration (1-20 µM). Colistin was effective starting from 5 µM at both E:T ratios (Fig. 4A), and increased cytotoxicity even at lower E:T ratios (Fig. 5). In contrast, the other compounds failed to elicit NK cell cytotoxicity in the tested conditions (Fig. 4B-H), indicating they were likely false positives. Taken together, these results corroborate that colistin sulfate enhances the cytotoxic activity of NK92 cells against K562 leukemia cells.

Colistin sulfate failed to potentiate NK cell killing of non-hematopoietic cancer cell lines.

K562 are widely used to study NK cell cytotoxicity due to their high susceptibility to NK recognition and killing. Given the promising results obtained with colistin, we tested if this compound would also increase NK-mediated killing of more resistant cell lines. For these studies, we employed the melanoma cell line A375 and the renal adenocarcinoma cell line 786O, both transduced with NL. Whereas killing of K562 was potentiated by drug treatment, neither A375 nor 786O cells were killed more effectively in the presence of colistin sulfate (Fig. 6), indicating that the compound failed to generally boost NK cell cytotoxicity.
The effect of colistin sulfate on NK cells is short lived.

To gather insights on the mechanisms underlying colistin-enhanced NK cell killing, we pre-treated NK92 cells with the drug for 24 hours and then employed them as effectors in killing assays. NK92 cells were pre-treated with 0, 1, 5 or 10 μM of colistin and, prior to incubation with K562-NL cells, the drug was washed out. Consistent with the results of our screening, colistin was not toxic towards NK92 cells (Fig. 7A). However, NK92 cells pre-treated with colistin failed to kill target cells more effectively than the control, whereas, consistent with what described above, colistin increased NK-mediated killing when present during the co-culture (Fig. 7B).

Considering that NK92 cells pre-treated for 24-hour with colistin did not present increased cytotoxicity, we tested if shorter pre-incubations could be more effective. NK92 cells were treated with 10 μM of colistin for 1 hour, and the drug was washed out prior to co-culture with K562-NL cells. In comparison to the untreated condition, 1-hour pre-treatment of NK92 cells with colistin slightly but consistently increased NK92 cytotoxicity (Fig. 7C). On the other hand, pre-treatment of K562 cells did not increase NK cell killing (Fig. 7D), suggesting that colistin sulfate, rather than sensitizing the target cells, acted on NK cells, but in a short-lived fashion.

Colistin sulfate increases cytotoxicity of primary human NK cells.

Lastly, we tested if colistin treatment increased cytotoxicity of primary NK cells. We obtained PBMCs from healthy donor blood and isolated NK cells by negative selection. NK cell purity was ~85% and both CD56+CD16- and CD56+CD16+ NK cell populations were present (not shown). After NK cells were isolated from PBMCs, they were immediately co-cultured with K562-NL cells at varying E:T ratios and treated with 10 μM of colistin for 5 hours. Pooled results from all 3
healthy donor are shown in Fig. 8. Consistent with the results obtained using NK92 cells, primary
NK cells treated with colistin showed an increased cytotoxicity towards K562-NL.

Overall, this screen of the Prestwick Chemical Library identified colistin as a potential enhancer
of NK cell cytotoxicity towards some cell types. The effect of colistin sulfate was short-lived but
was observed in both NK92 and primary human NK cells.
Discussion and Conclusions

Here, we conducted a high-throughput luciferase release-based cytotoxicity assay to screen the Prestwick Chemical Library and identify compounds that increased NK cell cytotoxicity. Luciferase-release assays have been used in previous a NK cell drug screening with success\textsuperscript{18}. The results of that screening identified small molecule inhibitors of NK cell cytotoxicity; however no small molecule enhancers were identified. To our knowledge, this is the first drug screening to employ a luciferase-release cytotoxicity assay format that identified small molecules capable of increasing NK cell cytotoxicity. Overall, the quality of our screening assay was fair, as determined by the Z’ factor. One problem we faced was that the dynamic range between the $<1:1 \text{ E:T DMSO negative control}>$ and $<9:1 \text{ E:T positive control}>$ in the 1:1 E:T plates decreased overtime, which is most likely due to decreased cytotoxicity of NK92 cells as time progressed. In preparation for the screen, we realized that cells kept at room temperature for more than 2-hours prior to co-culture for the cytotoxicity assay showed decreased cytotoxicity and therefore separated the screen in two days. However, the signal of the $<9:1 \text{ E:T positive control}>$ began to overlap with the signal of the $<1:1 \text{ E:T DMSO control}>$ and as a result reduced the Z’ factor. To improve future screenings, a strategy to maintain a low the signal-to-noise ratio overtime will be needed. Another limitation of the drug screening was that, due to COVID19-related shortage of plastic material, each compound was only tested in 2 biological replicates, which prevented us to perform a more robust statistical analysis of our results.

However, even in light of these limitations, the screening identified compounds previously reported to enhance NK cell activity, including amphotericin B\textsuperscript{19}. We also identified nicotinamide, which is currently under investigation in clinical trials as a supportive agent for ex vivo expansion.
of primary NK cells for the treatment of Non-Hodgkin lymphoma and multiple myeloma\textsuperscript{27}. Interestingly, nicotinamide failed to be validated in follow up experiments at the tested concentrations. On the other hand, two compounds identified in previous screens, naftifine and butenafine\textsuperscript{20}, were not highlighted in our screening (fold-change 0.84 and 1.14, respectively). Also, we identified monensin, a known inhibitor of NK cell degranulation as an enhancer of NK92 cytotoxicity. As expected, upon further tests, monensin was shown to decrease NK92 cytotoxicity in a dose-dependent manner.

From the 8 candidate drugs identified from screening of the Prestwick Chemical Library, colistin was the only drug that increased NK cell cytotoxicity in validation experiments. Colistin, also known as polymyxin E, is an antibiotic derived from \textit{Bacillus polymyxa} and is used to treat antibiotic-resistant infections\textsuperscript{28}. Colistin is an amphipathic molecule that disrupts the membrane of Gram-negative bacteria by displacing calcium and magnesium ions\textsuperscript{28}. This ultimately leads to increased cell permeability and eventually cell death. Few studies have investigated how colistin modulates immune cells, let alone NK cells. One study found that colistin increased cytotoxicity of murine splenic NK cells towards YAC-1 target cells and increased production of IFN-\gamma\textsuperscript{29}. Although no mechanism was provided, it was shown that both polycationic peptide and hydrophobic tail domains were needed for the observed effect\textsuperscript{29}. Colistin was also shown to increase NK cytotoxicity in combination with the antibiotics daptomycin or teicoplanin in mouse model of multi-resistant \textit{Acinetobacter baumannii} infection, and this combination showed a greater increase in NK cytotoxicity than either antibiotic on its own\textsuperscript{30}. Colistin was previously identified in a Prestwick Chemical Library screen as a compound capable of enhancing p38/MAPK pathway, a key pathway in innate immunity that is induced from TLR signaling\textsuperscript{31,32}. Subsequently,
this group showed that colistin increased phagocytosis, cytokine secretion and phosphorylation of p38 in rat macrophages and KEGG pathway analysis of treated macrophages showed upregulation of genes involved in signal transduction, immune pathways and calcium signaling\textsuperscript{33}. Interestingly, colistin induced upregulation of genes downstream of the MAPK and PI3K-Akt pathways\textsuperscript{33} in conditions similar to those of our screen. The MAPK and PI3K-Akt pathways are implicated in downstream signaling of NK activating receptors\textsuperscript{34}, suggesting a potential mechanism for colistin increasing NK cytotoxicity. Altogether, these highlighted studies illustrate that colistin has potential immunomodulatory properties beyond its bactericidal activity.

The fact that the effect of colistin was short-lived and evidence that some drugs disrupting membrane integrity have been shown to increase exocytosis of lytic granules of NK cells\textsuperscript{20}, suggests that colistin facilitated granule exocytosis in NK cells. However, if this was the mechanism of action, we would expect that colistin would increase NK cell-mediated killing towards all tested target cell lines, which was not the case. Therefore, the mechanism of action of colistin remains to be elucidated.

In conclusion, we first optimized a luciferase release-based NK cell cytotoxicity assay for a high-throughput format. Using this assay format, we screened the Prestwick Chemical Library for small molecules that had the ability to increase NK cell cytotoxicity and identified colistin sulfate salt as an enhancer of NK cell cytotoxicity.

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Author contributions.

Author contributions are detailed according to CRediT criteria.

| Author | Conceptualization | Formal analysis | Funding acquisition | Investigation | Methodology | Resources | Supervision | Visualization | Writing - original draft | Writing review & editing |
|--------|-------------------|-----------------|---------------------|---------------|-------------|-----------|-------------|---------------|-------------------------|------------------------|
| SCK    | X                 | X               | X                   | X             | X           | X         | X           | X             |                         |                        |
| MSH    |                   |                 |                     |               |             |           |             | X             |                         |                        |
| SK     |                   |                 |                     |               |             |           |             | X             |                         |                        |
| ZT     |                   | X               |                     |               |             |           |             | X             |                         |                        |
| GM     |                   |                 |                     |               |             |           |             | X             |                         |                        |
| SMC    |                   |                 | X                   |               |             |           |             | X             |                         |                        |
| SL     |                   |                 |                     |               |             |           |             | X             |                         |                        |
| JSD    | X                 | X               |                     | X             | X           | X         |             |               |                         |                        |
| MA     | X                 | X               | X                   |               |             | X         | X           | X             |                         |                        |

Conflicts of interest: JSD is an inventor on patents licensed to Turnstone Biologics, which is commercializing oncolytic Maraba virus. JSD has patents licensed and also holds equity in Virica Biotech, which is developing oncolytic virus platforms. MA has a consulting agreement with Alloy Therapeutics and a sponsored research agreement with Dragonfly Therapeutics and Actym Therapeutics.

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Figure Legends

Figure 1. Optimization of a luciferase release-based cytotoxicity assay for a high-throughput screen.

NK92 cells were co-cultured with K562-NL cells at the indicated E:T ratios for 5-hrs at 37°C. After incubation, the supernatant was collected, the indicated substrate added, and luminescence read by Biotek Synergy microplate reader. A. Luciferase-release cytotoxicity assay using transduced K562-NL cells (bulk population, unsorted). 20,000 K562-NL targets per well. After the incubation, luciferase activity was measured using Promega Nano-glo luciferase assay system. Mean +/- SD of three technical replicates. B. After the incubation, luciferase activity was measured after addition of either Promega Nano-glo luciferase assay system (FMZ) or CTZ substrate. 10,000 K562-NL targets per well. Mean +/- SD of three technical replicates. Representative of 3 biological replicates. C. Luciferase-release cytotoxicity assay using 10,000 K562-NL cells. After the incubation, luciferase activity was tested after addition of CTZ. Mean +/- SD of three technical replicates. Graph is representative of 2 biological replicates. D. K562-NL cells were treated with 30 μg/mL digitonin and compared to K562-NL cells co-cultured at a E:T ratio of 27. 10,000 K562-NL cells per well. Luciferase activity was tested after addition of CTZ. Mean +/- SD of three technical replicates. Representative of 2 biological replicates. E. Supernatant from a cytotoxicity assay was either collected directly or collected after a centrifugation step. Three technical replicates are shown. Representative of 2 biological replicates. F. NK92 or K562-NL cells were incubated at room temperature at indicated times (minutes) prior to start a cytotoxicity assay. Mean +/- SD of three technical replicates. Representative of 3 biological replicates.
Figure 2. Screening of the Prestwick Chemical Library.

A. Schematic workflow of the Prestwick Chemical Library screening. B. Average luminescent fold-change over DMSO control of all 1,200 compounds from NK92+K562-NL condition are plotted. The screening was conducted in singlet, over two biological replicates. The dotted red line indicates 1.3-fold-change. Compounds with a luminescent fold-change over DMSO control $\geq 1.3$ were considered enhancers of NK92 cytotoxicity. Points represent the average fold-change of n=2 biological replicates, except points 321-400 and 481-560 which represent fold-change from one replicate.

Figure 3. Colistin sulfate salt increases NK92 cytotoxicity against K562-NL.

NK92 and K562-NL cells were seeded into 96-well V bottom plates containing identified drug hits (10 μM) from the Prestwick Chemical Library at a E:T ratio of 1, with 10,000 K562-NL cells per well, for 5-hrs at 37°C. After the incubation, the supernatant was collected and transferred to 96-well black plates. A. Colistin sulfate salt. B. Nicotinamide. C. Diflorasone diacetate. D. Closantel. E. Benazepril hydrochloride. F. Tizanidine hydrochloride. G. monensin sodium salt. H. Zafirlukast. Mean +/- SD of n=2. Unpaired two-tailed Student’s t test. ns= not significant, **: p<0.01

Figure 4. Colistin sulfate salt increases NK92 cytotoxicity against K562-NL.

NK92 and K562-NL cells were seeded into a 96-well V bottom plate at a 1:1 or 3:1 E:T ratio with 10,000 K562-NL cells per well and treated with 1, 5, 10 and 20 μM of the indicated drug for 5-hrs at 37°C. After the incubation, the supernatant was collected and transferred to a 96-well black plate. A. Colistin sulfate salt. B. Nicotinamide. C. Diflorasone diacetate. D. Closantel. E.
Benazepril hydrochloride. **F.** Tizanidine hydrochloride. **G.** monensin sodium salt. **H.** Zafirlukast.

Mean +/- SD of n=2. Two-way ANOVA with Tukey’s multiple comparison test. **: p<0.01, ***: p<0.001, ****: p<0.0001.

**Figure 5. Treatment with colistin sulfate increases NK92 cytotoxicity against K562 cells.**

NK92 cells were mixed with K562-NL cells and seeded into a 96-well V bottom plate at a 0.3:1, 1:1 and 3:1 E:T ratio with 10,000 K562-NL cells per well and treated with 10 μM of colistin for 5-hrs at 37℃. After the incubation, the supernatant was collected and transferred to a 96-well black plate. The Biotek Synergy microplate reader was used to dispense CTZ and read luminescence. Percent specific lysis is depicted. Mean +/- SD of n=2. Statistical analysis with two-way ANOVA.

**Figure 6. Treatment with Colistin sulfate failed to increase NK92-mediated killing of non-hematopoietic cell lines.**

NK92 and K562-NL/A375-NL (A) or K562-NL/786O-NL (B) cells were seeded into a 96-well V bottom plate at a 1:1 E:T ratio with 10,000 target cells per well and treated with 10 μM of colistin for 5-hrs at 37℃. After the incubation, the supernatant was collected and transferred to a 96-well black plate. The Biotek Synergy microplate reader was used to dispense CTZ and read luminescence. Percent specific lysis is depicted. Mean +/- SD of n=2. Statistical analysis with two-tailed Student’s t-test. **: p<0.01; ****: p<0.0001.

**Figure 7. The effect of colistin sulfate on NK cells is short lived.**

A. Percent viability of NK92 cells by trypan-exclusion dye after 24-h treatment with 0, 1, 5, 10 μM of colistin. B NK92 cells were treated for 24-hrs with 0, 1, 5 and 10 μM of colistin. After
24-hrs, NK92 cells were washed and co-cultured with 10,000 K562-NL cells at a 1:1 E:T ratio for 5-hrs at 37°C. NK92 cells co-cultured with targets cells and treated with 10 μM of colistin during the 5-h incubation were also included. After the incubation, the supernatant was collected and transferred to a 96-well black plate. The Biotek Synergy microplate reader was used to dispense CTZ and read luminescence. Percent specific lysis is depicted. Mean +/- SD of n=3. One-way ANOVA with Dunnett’s multiple comparison test. ****: p<0.0001.

C. NK92 cells were treated for 1-h with 10 μM of colistin. After 1-h, the compound was washed and NK92 cells were co-cultured with 10,000 K562-NL cells in a 96-well V bottom plate at a 1:1 E:T ratio for 5-hrs at 37°C. NK92 cells co-cultured with targets cells and treated with 10 μM of colistin during the 5-h incubation were also included. After the incubation, the supernatant was collected and transferred to a 96-well black plate. The Biotek Synergy microplate reader was used to dispense CTZ and read luminescence. Percent specific lysis is depicted. Mean +/- SD of n=2. One-way ANOVA with Tukey’s multiple comparison test. ns= not significant, *: p<0.05, **: p<0.01; ****: p<0.0001.

D. NK92 and K562-NL cells were pre-treated separately with 10 μM of colistin. After 1-h, cells were washed and co-cultured with either treated or untreated cells. Cells were seeded in a 96-well V bottom plate at a E:T of 1 ratio using 10,000 K562-NL cells per well for 5-hrs at 37°C. NK92 cells co-cultured with targets cells and treated with 10 μM of colistin during the 5-h incubation were also included. After the incubation, the supernatant was collected and transferred to a 96-well black plate. The Biotek Synergy microplate reader was used to dispense CTZ and read luminescence. Percent specific lysis is depicted. Mean +/- SD of n=2. One-way ANOVA with Tukey’s multiple comparison test.
comparison test. Only significant differences between treatments are shown. *: p<0.05; ****:
p<0.0001.

**Figure 8. Colistin sulfate enhances the killing activity of primary human NK cells.**

Human NK cells isolated from PBMCs from healthy donors were mixed with K562-NL cells and were seeded into a 96-well V bottom plate at increasing E:T ratios, with 10,000 K562-NL cells per well and treated with 10 μM of colistin for 5-hrs at 37°C. After the incubation, the supernatant was collected and transferred to 96-well black plates. The Biotek Synergy microplate reader was used to dispense CTZ and read luminescence. Percent specific lysis is shown. Mean +/- SD of n=3 healthy donors. Statistical analysis was conducted with two-way ANOVA.

**Supplementary Figure 1: layout of the screening plates.**

**Supplementary Figure 2: generation of K562-NL:** K562 cells were transduced with a nano- luciferase expressing vector or a control and lysed. Luminescence was assessed (A). (B) K562-NL cells were sorted as single clones, and used as targets in cytotoxicity assays vis a vis with unsorted cells.
Figure 1
A

1. Dispense Prestwick Chemical Library and cells to assay plates.

   K562-NL + 10 uM drugs

   NK92 + K562-NL + 10 uM drugs

2. Treat with drugs for 5-hrs at 37C.

3. Transfer assay supernatant to read plates.

   collect supernatant

   Read plates

4. Dispense CTZ substrate and measure luminescence.

B

Specific lysis fold change

colistin sulfate salt

Figure 2
Figure 3

- **A**: Colistin sulfate
- **B**: Nicotinamide
- **C**: Diflorasone diacetate
- **D**: Closantel
- **E**: Benazepril hydrochloride
- **F**: Tizanidine hydrochloride
- **G**: Monensin sodium salt
- **H**: Zafirlukast

Legend:
- ns: Not significant
- ****: Significant at the 0.001 level
**Figure 4**

(A) % Specific Lysis vs. concentration (uM) for Colistin sulfate (E:T ratio 1:3).

(B) % Specific Lysis vs. concentration (uM) for Nicotinamide (E:T ratio 1:3).

(C) % Specific Lysis vs. concentration (uM) for Diflorasone diacetate (E:T ratio 1:3).

(D) % Specific Lysis vs. concentration (uM) for Closantel (E:T ratio 1:3).

(E) % Specific Lysis vs. concentration (uM) for Benazepril hydrochloride (E:T ratio 1:3).

(F) % Specific Lysis vs. concentration (uM) for Tizanidine hydrochloride (E:T ratio 1:3).

(G) % Specific Lysis vs. concentration (uM) for Monensin sodium salt (E:T ratio 1:3).

(H) % Specific Lysis vs. concentration (uM) for Zafirlukast (E:T ratio 1:3).
Figure 5

% Specific Lysis

p<0.0001

Colistin sulfate
untreated
Figure 6

A

K562-NL

A375-NL

% Specific Lysis

untreated

Colistin sulfate

untreated

Colistin sulfate

B

K562-NL

786O-NL

% Specific Lysis

untreated

Colistin sulfate

untreated

Colistin sulfate
Figure 7
Specific Lysis vs E:R ratio (E:R = 0.3:1, 1, 3) with treatments Colistin sulfate and untreated. 

Figure 8: Graph showing differences in % Specific Lysis between the two treatments with p<0.0001.
### Supplementary Figure 1

#### E:T=1

|     | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|-----|---|---|---|---|---|---|---|---|---|----|----|----|
| A   |   |   |   |   |   |   |   |   |   |    |    |    |
| B   |   |   |   |   |   |   |   |   |   |    |    |    |
| C   |   |   |   |   |   |   |   |   |   |    |    |    |
| D   |   |   |   |   |   |   |   |   |   |    |    |    |
| E   |   |   |   |   |   |   |   |   |   |    |    |    |
| F   |   |   |   |   |   |   |   |   |   |    |    |    |
| G   |   |   |   |   |   |   |   |   |   |    |    |    |
| H   |   |   |   |   |   |   |   |   |   |    |    |    |

10% DMSO    |   |   |   |   |   |   |   |   |   |    |    |    |

#### E:T=9

|     | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|-----|---|---|---|---|---|---|---|---|---|----|----|----|
| A   |   |   |   |   |   |   |   |   |   |    |    |    |
| B   |   |   |   |   |   |   |   |   |   |    |    |    |
| C   |   |   |   |   |   |   |   |   |   |    |    |    |
| D   |   |   |   |   |   |   |   |   |   |    |    |    |
| E   |   |   |   |   |   |   |   |   |   |    |    |    |
| F   |   |   |   |   |   |   |   |   |   |    |    |    |
| G   |   |   |   |   |   |   |   |   |   |    |    |    |
| H   |   |   |   |   |   |   |   |   |   |    |    |    |

10% DMSO    |   |   |   |   |   |   |   |   |   |    |    |    |

#### Targets alone

|     | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|-----|---|---|---|---|---|---|---|---|---|----|----|----|
| A   |   |   |   |   |   |   |   |   |   |    |    |    |
| B   |   |   |   |   |   |   |   |   |   |    |    |    |
| C   |   |   |   |   |   |   |   |   |   |    |    |    |
| D   |   |   |   |   |   |   |   |   |   |    |    |    |
| E   |   |   |   |   |   |   |   |   |   |    |    |    |
| F   |   |   |   |   |   |   |   |   |   |    |    |    |
| G   |   |   |   |   |   |   |   |   |   |    |    |    |
| H   |   |   |   |   |   |   |   |   |   |    |    |    |

10% DMSO    |   |   |   |   |   |   |   |   |   |    |    |    |

Digitonin   |   |   |   |   |   |   |   |   |   |    |    |    |

Supplementary Figure 1
Supplemental Table 1. Fold-change of NK92 and K562-NL cells treated with compounds from the Prestwick Chemical Library drug screening.

Fold-change of luminescent values of all wells containing compounds compared DMSO control wells in the same plate. Each compound was evaluated in singlet over 2 biological replicates. aPlates 5 & 7: fold-change of one replicate.

| Prestw number | Plate # / Well position | Chemical name                          | Target alone | 1:1 E:T |
|---------------|--------------------------|----------------------------------------|--------------|---------|
| Prestw-1      | 01A02                    | Azaguanine-8                           | 0.84         | 1.16    |
| Prestw-2      | 01A03                    | Allantoin                              | 0.86         | 1.15    |
| Prestw-3      | 01A04                    | Acetazolamide                          | 0.87         | 1.13    |
| Prestw-4      | 01A05                    | Metformin hydrochloride                | 0.86         | 1.16    |
| Prestw-5      | 01A06                    | Atracurium besylate                    | 0.83         | 1.15    |
| Prestw-6      | 01A07                    | Isoflupredone acetate                  | 0.76         | 1.19    |
| Prestw-7      | 01A08                    | Amiloride hydrochloride dihydrate      | 0.89         | 1.20    |
| Prestw-8      | 01A09                    | Amprolium hydrochloride                | 0.85         | 1.19    |
| Prestw-9      | 01A10                    | Hydrochlorothiazide                    | 0.81         | 1.20    |
| Prestw-10     | 01A11                    | Sulfaguanidine                         | 0.79         | 1.16    |
| Prestw-11     | 01B02                    | Meticrane                              | 0.86         | 1.05    |
| Prestw-12     | 01B03                    | Benzonatate                            | 0.81         | 1.16    |
| Prestw-13     | 01B04                    | Hydroflumethiazide                     | 0.92         | 1.16    |
| Prestw-14     | 01B05                    | Sulfacetamide sodic hydrate            | 0.83         | 1.09    |
| Prestw-15     | 01B06                    | Heptaminol hydrochloride               | 0.87         | 1.06    |
| Prestw-16     | 01B07                    | Sulfathiazole                          | 0.88         | 1.17    |
| Prestw-17     | 01B08                    | Levodopa                               | 0.86         | 1.12    |
| Prestw-18     | 01B09                    | Idoxuridine                            | 0.89         | 1.17    |
| Prestw-19     | 01B10                    | Captopril                              | 0.84         | 1.11    |
| Prestw-20     | 01B11                    | Minoxidil                              | 0.88         | 1.10    |
| Prestw-21 | 01C02 | Sulfaphenazole | 0.91 | 1.10 |
| Prestw-22 | 01C03 | Panthenol (D) | 0.97 | 1.15 |
| Prestw-23 | 01C04 | Sulfadiazine | 0.93 | 1.06 |
| Prestw-24 | 01C05 | Norethynodrel | 0.98 | 1.08 |
| Prestw-25 | 01C06 | Thiamphenicol | 0.91 | 1.11 |
| Prestw-26 | 01C07 | Cimetidine | 0.90 | 1.10 |
| Prestw-27 | 01C08 | Doxylamine succinate | 0.93 | 1.08 |
| Prestw-28 | 01C09 | Ethambutol dihydrochloride | 0.81 | 1.12 |
| Prestw-29 | 01C10 | Antipyrine | 0.80 | 1.00 |
| Prestw-30 | 01C11 | Antipyrine, 4-hydroxy | 0.83 | 1.10 |
| Prestw-31 | 01D02 | Chloramphenicol | 0.89 | 1.04 |
| Prestw-32 | 01D03 | Epirizole | 0.88 | 1.03 |
| Prestw-33 | 01D04 | Diprophylline | 0.85 | 1.04 |
| Prestw-34 | 01D05 | Triamterene | 0.92 | 1.08 |
| Prestw-35 | 01D06 | Dapsone | 0.94 | 1.08 |
| Prestw-36 | 01D07 | Troleandomycin | 0.91 | 1.15 |
| Prestw-37 | 01D08 | Pyrimethamine | 0.82 | 1.06 |
| Prestw-38 | 01D09 | Hexamethonium dibromide dihydrate | 0.89 | 1.13 |
| Prestw-39 | 01D10 | Diflunisal | 0.79 | 1.06 |
| Prestw-40 | 01D11 | Niclosamide | 0.81 | 1.18 |
| Prestw-41 | 01E02 | Procaine hydrochloride | 0.92 | 1.07 |
| Prestw-42 | 01E03 | Moxisylyte hydrochloride | 0.94 | 1.10 |
| Prestw-43 | 01E04 | Betazole hydrochloride | 0.95 | 1.06 |
| Prestw-44 | 01E05 | Isoxicam | 0.91 | 1.00 |
| Prestw-45 | 01E06 | Naproxen | 0.91 | 1.05 |
| Prestw-46 | 01E07 | Naphazoline hydrochloride | 0.92 | 1.08 |
| Prestw-47 | 01E08 | Ticlopidine hydrochloride | 0.88 | 1.12 |
| Prestw-48 | 01E09 | Dicyclomine hydrochloride | 0.89 | 1.05 |
| Prestw-49 | 01E10 | Amyleine hydrochloride | 0.84 | 1.04 |
| Prestw-50 | 01E11 | Lidocaïne hydrochloride | 0.92 | 1.04 |
| Prestw-51 | 01F02 | Trichlorfon | 0.93 | 0.99 |
| Prestw-52 | 01F03 | Carbamazepine | 0.95 | 1.02 |
| Prestw-53 | 01F04 | Triflupromazine hydrochloride | 0.94 | 0.96 |
| Prestw-54 | 01F05 | Mefenamic acid | 0.91 | 1.05 |
| Prestw-55 | 01F06 | Acetohexamide | 0.95 | 1.06 |
| Prestw-56 | 01F07 | Sulpiride | 0.93 | 1.02 |
| Prestw-57 | 01F08 | Benoxinate hydrochloride | 0.85 | 1.00 |
| Prestw-58 | 01F09 | Oxethazaine | 0.82 | 1.01 |
| Prestw-59 | 01F10 | Pheniramine maleate | 0.80 | 1.13 |
| Prestw-60 | 01F11 | Tolazoline hydrochloride | 0.81 | 1.02 |
| Prestw-61 | 01G02 | Morantel tartrate | 0.87 | 1.00 |
| Prestw-62 | 01G03 | Homatropine hydrobromide (R,S) | 0.89 | 0.99 |
| Prestw-63 | 01G04 | Nifedipine | 0.79 | 1.03 |
| Code     | Identifier | Name                        | Value 1 | Value 2 |
|----------|------------|-----------------------------|---------|---------|
| Prestw-64| 01G05      | Chlorpromazine hydrochloride | 0.91    | 1.01    |
| Prestw-65| 01G06      | Diphenhydramine hydrochloride | 0.77    | 0.96    |
| Prestw-66| 01G07      | Minaprine dihydrochloride   | 0.83    | 1.03    |
| Prestw-67| 01G08      | Miconazole                  | 0.85    | 1.06    |
| Prestw-68| 01G09      | Isoxsuprine hydrochloride   | 0.84    | 1.00    |
| Prestw-69| 01G10      | Acebutolol hydrochloride    | 0.85    | 1.02    |
| Prestw-70| 01G11      | Tolnaftate                  | 0.85    | 1.06    |
| Prestw-71| 01H02      | Todralazine hydrochloride   | 0.82    | 1.02    |
| Prestw-72| 01H03      | Imipramine hydrochloride    | 0.81    | 0.91    |
| Prestw-73| 01H04      | Sulindac                    | 0.83    | 0.99    |
| Prestw-74| 01H05      | Amitryptiline hydrochloride | 0.90    | 0.91    |
| Prestw-75| 01H06      | Adiphenine hydrochloride    | 0.87    | 1.01    |
| Prestw-76| 01H07      | Dibucaine                   | 0.87    | 0.99    |
| Prestw-77| 01H08      | Prednisone                  | 0.85    | 1.02    |
| Prestw-78| 01H09      | Thioridazine hydrochloride  | 0.82    | 0.98    |
| Prestw-79| 01H10      | Diphemanil methylsulfate    | 0.72    | 0.99    |
| Prestw-80| 01H11      | Trimethobenzamine hydrochloride | 0.84  | 1.06    |
| Plate 2  |            |                             |         |         |
| Prestw-81| 02A02      | Metronidazole               | 0.89    | 1.16    |
| Prestw-82| 02A03      | Fulvestrant                 | 0.97    | 1.16    |
| Prestw-83| 02A04      | Edrophonium chloride        | 0.92    | 1.24    |
| Prestw-84| 02A05      | Moroxidine hydrochloride    | 0.83    | 1.13    |
| Prestw-85| 02A06      | Baclofen (R,S)              | 0.94    | 1.13    |
| Prestw-86| 02A07      | Acyclovir                   | 0.95    | 1.17    |
| Prestw-87| 02A08      | Diazoxide                   | 0.91    | 1.19    |
| Prestw-88| 02A09      | Amidopyrine                 | 0.93    | 1.12    |
| Prestw-89| 02A10      | Busulfan                    | 0.90    | 1.20    |
| Prestw-90| 02A11      | Pindolol                    | 0.91    | 1.19    |
| Prestw-91| 02B02      | Khellin                     | 0.86    | 1.03    |
| Prestw-92| 02B03      | Zimelidine dihydrochloride monohydrate | 0.92  | 1.08    |
| Prestw-93| 02B04      | Azacyclonol                 | 0.86    | 1.03    |
| Prestw-94| 02B05      | Azathioprine                | 0.89    | 1.07    |
| Prestw-95| 02B06      | Lynestrenol                 | 0.90    | 1.10    |
| Prestw-96| 02B07      | Guanabenz acetate           | 0.95    | 1.19    |
| Prestw-97| 02B08      | Disulfiram                  | 0.95    | 0.87    |
| Prestw-98| 02B09      | Acetylsalicylsalicyclic acid | 0.93  | 1.23    |
| Prestw-99| 02B10      | Mianserine hydrochloride    | 0.96    | 1.08    |
| Prestw-100| 02B11     | Nocodazole                  | 0.99    | 1.25    |
| Code   | Description                                      | Value1 | Value2 |
|--------|-------------------------------------------------|--------|--------|
| Prestw-101 | R(-) Apomorphine hydrochloride hemihydrate          | 0.89   | 1.10   |
| Prestw-102 | Amoxapine                                         | 0.87   | 0.86   |
| Prestw-103 | Cyproheptadine hydrochloride                      | 0.84   | 1.09   |
| Prestw-104 | Famotidine                                        | 0.88   | 1.16   |
| Prestw-105 | Danazol                                           | 0.98   | 1.07   |
| Prestw-106 | Nicorandil                                        | 0.93   | 1.14   |
| Prestw-1314 | Pioglitazone                                      | 1.02   | 1.16   |
| Prestw-108 | Nomifensine maleate                               | 0.89   | 1.04   |
| Prestw-109 | Dizocilpine maleate                               | 0.86   | 1.04   |
| Prestw-1192 | Oxandrolone                                        | 0.83   | 1.16   |
| Prestw-111 | Naloxone hydrochloride                             | 0.94   | 1.08   |
| Prestw-112 | Metolozone                                         | 0.80   | 1.01   |
| Prestw-113 | Ciprofloxacin hydrochloride                        | 0.93   | 1.02   |
| Prestw-114 | Ampicillin trihydrate                              | 0.91   | 1.06   |
| Prestw-115 | Haloperidol                                        | 0.95   | 1.06   |
| Prestw-116 | Naltrexone hydrochloride dihydrate                 | 0.90   | 1.06   |
| Prestw-117 | Chlorpheniramine maleate                           | 0.90   | 1.00   |
| Prestw-118 | Nalbuphine hydrochloride                           | 0.85   | 1.05   |
| Prestw-119 | Picotamide monohydrate                             | 0.83   | 1.13   |
| Prestw-120 | Triamcinolone                                      | 0.81   | 1.14   |
| Prestw-121 | Bromocryptine mesylate                             | 0.85   | 1.24   |
| Prestw-1471 | Amfepramone hydrochloride                          | 0.93   | 1.08   |
| Prestw-123 | Dehydrocholic acid                                 | 0.93   | 1.15   |
| Code    | Name                          | Value1 | Value2 |
|---------|-------------------------------|--------|--------|
| Prestw-1184 | Tioconazole                  | 0.94   | 0.98   |
| Prestw-125   | Perphenazine                  | 0.98   | 0.45   |
| Prestw-126   | Mefloquine hydrochloride      | 0.95   | 1.03   |
| Prestw-127   | Isoconazole                   | 0.88   | 1.04   |
| Prestw-128   | Spironolactone                | 0.86   | 1.11   |
| Prestw-129   | Pirenzepine dihydrochloride   | 0.88   | 1.09   |
| Prestw-130   | Dexamethasone acetate         | 0.88   | 1.13   |
| Prestw-131   | Glipizide                     | 0.86   | 1.07   |
| Prestw-132   | Loxapine succinate           | 0.78   | 0.90   |
| Prestw-133   | Hydroxyzine dihydrochloride   | 0.77   | 0.80   |
| Prestw-134   | Diltiazem hydrochloride       | 1.00   | 1.03   |
| Prestw-135   | Methotrexate                  | 0.88   | 1.10   |
| Prestw-136   | Astemizole                    | 0.94   | 0.77   |
| Prestw-137   | Clindamycin hydrochloride     | 0.92   | 1.08   |
| Prestw-138   | Terfenadine                   | 1.10   | 0.86   |
| Prestw-139   | Cefotaxime sodium salt        | 0.93   | 1.11   |
| Prestw-140   | Tetracycline hydrochloride    | 0.84   | 1.14   |
| Prestw-141   | Verapamil hydrochloride       | 0.87   | 0.99   |
| Prestw-142   | Dipyridamole                  | 0.93   | 1.03   |
| Prestw-143   | Chlorhexidine                 | 1.36   | 0.41   |
| Prestw-144   | Loperamide hydrochloride      | 0.93   | 0.83   |
| Prestw-145   | Chlortetracycline hydrochloride| 0.91   | 1.03   |
| Prestw-146   | Tamoxifen citrate             | 0.87   | 1.00   |
| Code     | Code     | Substance                          | Unit 1 | Unit 2 |
|----------|----------|------------------------------------|--------|--------|
| Prestw-147 | 02G08    | Nicergoline                        | 0.90   | 1.03   |
| Prestw-148 | 02G09    | Canrenoic acid potassium salt      | 0.87   | 1.01   |
| Prestw-149 | 02G10    | Thioproperazine dimesylate          | 0.86   | 0.77   |
| Prestw-150 | 02G11    | Dihydroergotamine tartrate         | 0.89   | 0.82   |
| Prestw-151 | 02H02    | Erythromycin                       | 0.76   | 0.95   |
| Prestw-1474 | 02H03   | Chloroxine                         | 0.84   | 0.97   |
| Prestw-153 | 02H04    | Didanosine                         | 0.87   | 0.97   |
| Prestw-154 | 02H05    | Josamycin                          | 0.87   | 0.97   |
| Prestw-155 | 02H06    | Paclitaxel                         | 0.82   | 0.94   |
| Prestw-156 | 02H07    | Ivermectin                         | 0.79   | 1.05   |
| Prestw-157 | 02H08    | Gallamine triethiodide             | 0.79   | 0.95   |
| Prestw-158 | 02H09    | Neomycin sulfate                   | 0.87   | 1.02   |
| Prestw-159 | 02H10    | Dihydrostreptomycin sulfate        | 0.85   | 1.01   |
| Prestw-160 | 02H11    | Gentamicine sulfate                | 0.89   | 1.06   |
| Plate 3   |          |                                    |        |        |
| Prestw-161 | 03A02    | Isoniazid                          | 0.90   | 1.10   |
| Prestw-162 | 03A03    | Pentylenetetrazole                 | 0.95   | 1.14   |
| Prestw-163 | 03A04    | Chlorzoxazone                      | 0.89   | 1.09   |
| Prestw-164 | 03A05    | Ornidazole                         | 0.86   | 1.17   |
| Prestw-165 | 03A06    | Ethosuximide                       | 0.94   | 1.08   |
| Prestw-166 | 03A07    | Mafenide hydrochloride             | 0.97   | 1.22   |
| Prestw-167 | 03A08    | Riluzole hydrochloride             | 0.95   | 0.94   |
| Prestw-168 | 03A09    | Nitrofurantoin                     | 0.91   | 1.11   |
| Reference  | Code   | Name                        | Lower Limit | Upper Limit |
|-----------|--------|-----------------------------|-------------|-------------|
| Prestw-169| 03A10  | Hydralazine hydrochloride   | 0.87        | 1.14        |
| Prestw-170| 03A11  | Phenelzine sulfate          | 0.96        | 1.26        |
| Prestw-171| 03B02  | Tranexamic acid             | 0.86        | 1.04        |
| Prestw-172| 03B03  | Etofylline                  | 1.01        | 1.18        |
| Prestw-173| 03B04  | Tranylcypromine hydrochloride | 0.90 | 1.07        |
| Prestw-174| 03B05  | Alverine citrate salt       | 0.97        | 1.10        |
| Prestw-175| 03B06  | Aceclofenac                 | 0.92        | 1.07        |
| Prestw-176| 03B07  | Iproniazide phosphate       | 0.88        | 1.14        |
| Prestw-177| 03B08  | Sulfamethoxazole            | 0.84        | 1.02        |
| Prestw-178| 03B09  | Mephenesin                  | 0.90        | 1.07        |
| Prestw-179| 03B10  | Phenformin hydrochloride    | 0.86        | 1.12        |
| Prestw-180| 03B11  | Flutamide                   | 0.96        | 0.96        |
| Prestw-181| 03C02  | Ampyrone                    | 0.93        | 1.05        |
| Prestw-182| 03C03  | Levamisole hydrochloride    | 0.84        | 0.94        |
| Prestw-183| 03C04  | Pargyline hydrochloride     | 0.83        | 1.03        |
| Prestw-184| 03C05  | Methocarbamol               | 0.95        | 1.08        |
| Prestw-185| 03C06  | Aztreonam                   | 0.86        | 1.06        |
| Prestw-186| 03C07  | Cloxacillin sodium salt     | 0.88        | 1.02        |
| Prestw-187| 03C08  | Catharanthine               | 0.89        | 1.06        |
| Prestw-188| 03C09  | Pentolinium bitartrate      | 0.85        | 1.02        |
| Prestw-189| 03C10  | Aminopurine, 6-benzyl       | 0.69        | 0.85        |
| Prestw-190| 03C11  | Tolbutamide                 | 0.88        | 0.84        |
| Prestw-191| 03D02  | Midodrine hydrochloride     | 0.87        | 0.96        |
| Code   | Name                                           | Value1 | Value2 |
|--------|------------------------------------------------|--------|--------|
| Prestw-192 | 03D03 Thalidomide                              | 0.88   | 0.94   |
| Prestw-193 | 03D04 Oxolinic acid                            | 0.94   | 0.98   |
| Prestw-194 | 03D05 Nimesulide                               | 0.90   | 1.06   |
| Prestw-195 | 03D06 Hydrastinine hydrochloride               | 0.85   | 0.98   |
| Prestw-196 | 03D07 Pentoxifylline                           | 0.93   | 0.97   |
| Prestw-197 | 03D08 Metaraminol bitartrate                  | 0.85   | 0.99   |
| Prestw-198 | 03D09 Salbutamol                               | 0.86   | 1.11   |
| Prestw-199 | 03D10 Prilocaine hydrochloride                | 0.91   | 0.99   |
| Prestw-200 | 03D11 Camptothecine (S,+)                     | 0.88   | 0.87   |
| Prestw-201 | 03E02 Ranitidine hydrochloride                | 0.90   | 1.11   |
| Prestw-202 | 03E03 Tiratricol, 3,3',5-triiodothyroacetic acid | 0.83   | 1.06   |
| Prestw-203 | 03E04 Flufenamic acid                          | 0.92   | 1.05   |
| Prestw-204 | 03E05 Flumequine                               | 0.98   | 1.09   |
| Prestw-205 | 03E06 Tolfenamic acid                          | 0.90   | 1.10   |
| Prestw-206 | 03E07 Meclofenamic acid sodium salt monohydrate | 0.85   | 1.06   |
| Prestw-1181 | 03E08 Tibolone                                | 1.04   | 1.02   |
| Prestw-208 | 03E09 Trimethoprim                             | 0.94   | 1.03   |
| Prestw-209 | 03E10 Metoclopramide monohydrochloride         | 0.87   | 1.03   |
| Prestw-210 | 03E11 Fenbendazole                             | 0.90   | 0.90   |
| Prestw-211 | 03F02 Piroxicam                                | 0.92   | 0.94   |
| Prestw-212 | 03F03 Pyrantel tartrate                        | 0.86   | 0.93   |
| Prestw-213 | 03F04 Fenspiride hydrochloride                 | 0.93   | 0.97   |
| Prestw-214 | 03F05 Gemfibrozil                              | 0.87   | 0.95   |
| Code   | Description                          | Value 1 | Value 2 |
|--------|--------------------------------------|---------|---------|
| Prestw-215 | Mefexamide hydrochloride             | 0.85    | 0.97    |
| Prestw-216 | Tiapride hydrochloride               | 0.92    | 1.05    |
| Prestw-217 | Mebendazole                          | 0.91    | 1.03    |
| Prestw-218 | Fenbufen                             | 0.86    | 1.03    |
| Prestw-219 | Ketoprofen                           | 0.88    | 0.96    |
| Prestw-220 | Indapamidine                         | 0.88    | 1.01    |
| Prestw-221 | Norfloxacin                          | 0.82    | 1.01    |
| Prestw-222 | Antimycin A                          | 0.95    | 1.15    |
| Prestw-223 | Xylometazoline hydrochloride         | 0.87    | 1.00    |
| Prestw-224 | Oxymetazoline hydrochloride          | 0.89    | 1.02    |
| Prestw-225 | Nifenazone                           | 0.87    | 0.95    |
| Prestw-226 | Griseofulvin                         | 0.75    | 0.95    |
| Prestw-227 | Clemizole hydrochloride              | 0.88    | 1.02    |
| Prestw-228 | Tropicamide                          | 0.86    | 0.83    |
| Prestw-229 | Nefopam hydrochloride                | 0.88    | 0.70    |
| Prestw-230 | Phentolamine hydrochloride           | 0.86    | 0.75    |
| Prestw-231 | Etodolac                             | 0.92    | 1.07    |
| Prestw-232 | Scopolamin-N-oxide hydrobromide      | 0.95    | 0.97    |
| Prestw-233 | Hyoscyamine (L)                      | 0.95    | 1.01    |
| Prestw-234 | Chlorphensin carbamate               | 0.92    | 0.99    |
| Prestw-235 | Metampicillin sodium salt            | 0.92    | 0.94    |
| Prestw-236 | Dilazep dihydrochloride              | 0.95    | 1.01    |
| Prestw-237 | Ofloxacin                            | 0.97    | 1.05    |
|   |   |   |   |   |   |
|---|---|---|---|---|---|
| Prestw- | 03H09 | Lomefloxacin hydrochloride | 0.96 | 1.03 |
| Prestw- | 03H10 | Orphenadrine hydrochloride | 0.95 | 0.91 |
| Prestw- | 03H11 | Proglumide | 0.85 | 1.08 |
| Plate 4 |   |   |   |   |   |
| Prestw- | 04A02 | Mexiletine hydrochloride | 0.91 | 1.20 |
| Prestw- | 04A03 | Flavoxate hydrochloride | 0.84 | 1.16 |
| Prestw- | 04A04 | Bufexamac | 0.85 | 1.09 |
| Prestw- | 04A05 | Glutethimide, para-amino | 0.96 | 1.22 |
| Prestw- | 04A06 | Dropropizine (R,S) | 0.89 | 1.21 |
| Prestw- | 04A07 | Pinacidil | 0.92 | 1.03 |
| Prestw- | 04A08 | Albendazole | 0.92 | 1.02 |
| Prestw- | 04A09 | Clonidine hydrochloride | 0.86 | 1.20 |
| Prestw- | 04A10 | Bupropion hydrochloride | 0.86 | 1.29 |
| Prestw- | 04A11 | Alprenolol hydrochloride | 0.90 | 1.18 |
| Prestw- | 04B02 | Chlorothiazide | 0.82 | 0.95 |
| Prestw- | 04B03 | Diphenidol hydrochloride | 0.78 | 1.10 |
| Prestw- | 04B04 | Norethindrone | 0.80 | 1.13 |
| Prestw- | 04B05 | Nortriptyline hydrochloride | 0.80 | 0.99 |
| Prestw- | 04B06 | Niflumic acid | 0.82 | 1.17 |
| Prestw- | 04B07 | Isotretinoin | 0.84 | 1.23 |
| Prestw- | 04B08 | Retinoic acid | 0.89 | 1.24 |
| Prestw- | 04B09 | Antazoline hydrochloride | 0.83 | 1.11 |
| Prestw- | 04B10 | Ethacrynic acid | 0.89 | 1.20 |
| Code     | Name                              | Min | Max |
|----------|-----------------------------------|-----|-----|
| Prestw-260 | Praziquantel                      | 0.86| 1.10|
| Prestw-261 | Ethisterone                       | 0.81| 1.04|
| Prestw-262 | Triprolidine hydrochloride        | 0.83| 1.12|
| Prestw-263 | Doxepin hydrochloride             | 0.86| 0.86|
| Prestw-264 | Dyclonine hydrochloride           | 0.76| 1.01|
| Prestw-265 | Dimenhydrinate                    | 0.82| 1.09|
| Prestw-266 | Disopyramide                      | 0.87| 1.14|
| Prestw-267 | Clotrimazole                      | 0.92| 1.06|
| Prestw-268 | Vinpocetine                       | 0.86| 1.25|
| Prestw-269 | Clomipramine hydrochloride        | 0.84| 0.97|
| Prestw-270 | Fendiline hydrochloride           | 0.89| 0.91|
| Prestw-271 | Vincamine                         | 0.82| 1.12|
| Prestw-272 | Indomethacin                      | 0.83| 1.02|
| Prestw-273 | Cortisone                         | 0.78| 1.11|
| Prestw-274 | Prednisolone                      | 0.98| 1.16|
| Prestw-275 | Fenofibrate                       | 0.82| 1.12|
| Prestw-276 | Bumetanide                        | 0.88| 1.25|
| Prestw-277 | Labetalol hydrochloride           | 0.84| 1.09|
| Prestw-278 | Cinnarizine                       | 0.86| 1.18|
| Prestw-279 | Methylprednisolone, 6-alpha       | 0.80| 1.26|
| Prestw-280 | Quinidine hydrochloride monohydrate | 0.80| 1.14|
| Prestw-281 | Fludrocortisone acetate           | 0.81| 1.11|
| Prestw-282 | Fenoterol hydrobromide            | 0.82| 1.15|
| Code   | Name                                      | Value1 | Value2 |
|--------|-------------------------------------------|--------|--------|
| 04E04  | Homochlorcyclizine dihydrochloride         | 0.72   | 0.81   |
| 04E05  | Diethylcarbamazine citrate                | 0.78   | 1.19   |
| 04E06  | Chenodiol                                 | 0.86   | 1.13   |
| 04E07  | Perhexiline maleate                       | 0.82   | 0.80   |
| 04E08  | Oxybutynin chloride                       | 0.81   | 1.06   |
| 04E09  | Spiperone                                 | 0.86   | 1.14   |
| 04E10  | Pyrilamine maleate                        | 0.83   | 1.13   |
| 04E11  | Sulfinpyrazone                            | 0.77   | 1.09   |
| 04F02  | Dantrolene sodium salt                    | 0.73   | 0.97   |
| 04F03  | Trazodone hydrochloride                   | 0.71   | 0.96   |
| 04F04  | Glafenine hydrochloride                   | 0.79   | 1.09   |
| 04F05  | Pimethixene maleate                       | 0.73   | 0.81   |
| 04F06  | Pergolide mesylate                        | 0.85   | 1.26   |
| 04F07  | Acemetacin                                | 0.77   | 1.05   |
| 04F08  | Benzydamine hydrochloride                 | 0.83   | 0.99   |
| 04F09  | Fipexide hydrochloride                    | 0.84   | 1.17   |
| 04F10  | Mifepristone                              | 0.84   | 1.17   |
| 04F11  | Diperodon hydrochloride                   | 0.81   | 1.01   |
| 04G02  | Lisinopril                                | 0.80   | 0.96   |
| 04G03  | Lincomycin hydrochloride                  | 0.79   | 1.04   |
| 04G04  | Telenzepine dihydrochloride               | 0.80   | 1.06   |
| 04G05  | Econazole nitrate                         | 0.81   | 1.21   |
| 04G06  | Bupivacaine hydrochloride                 | 0.80   | 1.26   |
| Prestw-306 | 04G07  | Clemastine fumarate | 0.77 | 0.86 |
| Prestw-307 | 04G08  | Oxytetracycline dihydrate | 0.84 | 1.29 |
| Prestw-308 | 04G09  | Pimozide | 0.85 | 1.16 |
| Prestw-309 | 04G10  | Amodiaquin dihydrochloride dihydrate | 0.89 | 0.72 |
| Prestw-310 | 04G11  | Mebeverine hydrochloride | 0.84 | 1.19 |
| Prestw-311 | 04H02  | Ifenprodil tartrate | 0.75 | 0.98 |
| Prestw-312 | 04H03  | Flunarizine dihydrochloride | 0.78 | 1.17 |
| Prestw-313 | 04H04  | Trifluoperazine dihydrochloride | 0.79 | 0.78 |
| Prestw-314 | 04H05  | Enalapril maleate | 0.85 | 1.05 |
| Prestw-315 | 04H06  | Minocycline hydrochloride | 0.83 | 1.04 |
| Prestw-316 | 04H07  | Glibenclamide | 0.81 | 1.19 |
| Prestw-317 | 04H08  | Guanethidine sulfate | 0.82 | 1.07 |
| Prestw-318 | 04H09  | Quinacrine dihydrochloride dihydrate | 0.85 | 0.47 |
| Prestw-319 | 04H10  | Clofilium tosylate | 0.85 | 1.08 |
| Prestw-320 | 04H11  | Fluphenazine dihydrochloride | 0.85 | 0.76 |

**Plate 5**

| Prestw-321 | 05A02  | Streptomycin sulfate | 1.03 | 1.09 |
| Prestw-322 | 05A03  | Alfuzosin hydrochloride | 1.00 | 1.14 |
| Prestw-323 | 05A04  | Chlorpropamide<sup>a</sup> | 1.04 | 1.09 |
| Prestw-324 | 05A05  | Phenylpropanolamine hydrochloride | 1.03 | 1.08 |
| Prestw-325 | 05A06  | Ascorbic acid | 1.13 | 1.10 |
| Prestw-326 | 05A07  | Methyldopa (L,−) | 1.08 | 1.12 |
| Prestw-327 | 05A08  | Cefoperazone dihydrate | 1.04 | 1.09 |
| Prestw-328 | 05A09  | Zoxazolamine         | 0.97 | 1.17 |
| Prestw-329 | 05A10  | Tacrine hydrochloride hydrate | 0.92 | 1.07 |
| Prestw-330 | 05A11  | Bisoprolol fumarate | 0.97 | 1.27 |
| Prestw-331 | 05B02  | Tremorine dihydrochloride | 0.87 | 0.79 |
| Prestw-332 | 05B03  | Practolol | 0.89 | 0.93 |
| Prestw-333 | 05B04  | Zidovudine, AZT | 0.97 | 0.93 |
| Prestw-334 | 05B05  | Sulfisoxazole | 0.94 | 0.97 |
| Prestw-335 | 05B06  | Zaprinast | 1.04 | 1.02 |
| Prestw-336 | 05B07  | Chlormezanone | 0.92 | 0.91 |
| Prestw-337 | 05B08  | Procainamide hydrochloride | 0.93 | 0.98 |
| Prestw-338 | 05B09  | N6-methyladenosine | 0.97 | 1.00 |
| Prestw-339 | 05B10  | Guanfacine hydrochloride | 1.44 | 1.05 |
| Prestw-340 | 05B11  | Domperidone | 0.92 | 0.62 |
| Prestw-341 | 05C02  | Furosemide | 0.93 | 0.93 |
| Prestw-342 | 05C03  | Methapyrilene hydrochloride | 0.90 | 0.96 |
| Prestw-343 | 05C04  | Desipramine hydrochloride | 0.78 | 0.65 |
| Prestw-344 | 05C05  | Clorgyline hydrochloride | 0.88 | 0.98 |
| Prestw-345 | 05C06  | Clenbuterol hydrochloride | 0.96 | 0.94 |
| Prestw-346 | 05C07  | Maprotiline hydrochloride | 0.99 | 0.78 |
| Prestw-347 | 05C08  | Thioguanosine | 0.96 | 1.04 |
| Prestw-348 | 05C09  | Chlorprothixene hydrochloride | 0.93 | 0.88 |
| Prestw-349 | 05C10  | Ritodrine hydrochloride | 1.69 | 1.03 |
| Prestw-350 | 05C11  | Clozapine | 0.96 | 0.73 |
| Prestw-351  | 05D02 | Chlorthalidone | 0.91 | 0.88 |
| Prestw-352  | 05D03 | Dobutamine hydrochloride | 0.86 | 0.91 |
| Prestw-353  | 05D04 | Moclobemide | 0.95 | 1.00 |
| Prestw-354  | 05D05 | Clopamide | 0.98 | 0.94 |
| Prestw-355  | 05D06 | Hycanthone | 0.93 | 0.74 |
| Prestw-356  | 05D07 | Adenosine 5'-monophosphate monohydrate | 1.03 | 1.12 |
| Prestw-357  | 05D08 | Amoxicillin | 1.05 | 1.22 |
| Prestw-358  | 05D09 | Cephalexin monohydrate | 1.07 | 1.17 |
| Prestw-359  | 05D10 | Dextromethorphan hydrobromide monohydrate | 1.09 | 1.01 |
| Prestw-360  | 05D11 | Droperidol | 1.04 | 0.95 |
| Prestw-361  | 05E02 | Bambuterol hydrochloride | 0.97 | 0.88 |
| Prestw-362  | 05E03 | Betamethasone | 0.95 | 1.09 |
| Prestw-363  | 05E04 | Colchicine | 1.01 | 0.38 |
| Prestw-364  | 05E05 | Metergoline | 1.08 | 0.94 |
| Prestw-365  | 05E06 | Brinzolamide | 1.02 | 0.98 |
| Prestw-366  | 05E07 | Ambroxol hydrochloride | 0.98 | 1.13 |
| Prestw-367  | 05E08 | Benfluorex hydrochloride | 0.99 | 1.09 |
| Prestw-368  | 05E09 | Bepridil hydrochloride | 0.96 | 0.99 |
| Prestw-369  | 05E10 | Meloxicam | 1.50 | 0.98 |
| Prestw-370  | 05E11 | Benzbromarone | 1.01 | 0.94 |
| Prestw-371  | 05F02 | Ketonofen fumarate | 0.88 | 0.78 |
| Prestw-372  | 05F03 | Debrisoquin sulfate | 0.98 | 0.99 |
| Prestw-373  | 05F04 | Amethopterin (R,S) | 0.97 | 1.07 |
| Prestw-374 | 05F05 | Methylergometrine maleate | 1.09 | 0.99 |
| Prestw-375 | 05F06 | Methiothepin maleate | 1.14 | 0.63 |
| Prestw-376 | 05F07 | Clofazimine | 0.98 | 0.98 |
| Prestw-377 | 05F08 | Nafronyl oxalate | 1.09 | 1.14 |
| Prestw-378 | 05F09 | Bezafibrate | 1.02 | 1.12 |
| Prestw-1152 | 05F10 | Nefazodone HCl | 1.34 | 1.04 |
| Prestw-380 | 05F11 | Clebopride maleate | 1.12 | 0.80 |
| Prestw-381 | 05G02 | Lidoflazine | 0.80 | 0.53 |
| Prestw-382 | 05G03 | Betaxolol hydrochloride | 1.00 | 0.96 |
| Prestw-383 | 05G04 | Nicardipine hydrochloride | 0.36 | 0.45 |
| Prestw-384 | 05G05 | Probucol | 0.95 | 1.02 |
| Prestw-385 | 05G06 | Mitoxantrone dihydrochloride | 1.05 | 0.87 |
| Prestw-386 | 05G07 | GBR 12909 dihydrochloride | 0.98 | 0.96 |
| Prestw-387 | 05G08 | Carbetapentane citrate | 1.00 | 1.05 |
| Prestw-388 | 05G09 | Dequalinium dichloride | 1.12 | 0.69 |
| Prestw-389 | 05G10 | Ketoconazole | 1.00 | 0.85 |
| Prestw-390 | 05G11 | Fusidic acid sodium salt | 1.04 | 0.76 |
| Prestw-391 | 05H02 | Terbutaline hemisulfate | 0.91 | 1.01 |
| Prestw-392 | 05H03 | Ketanserin tartrate hydrate | 0.90 | 1.02 |
| Prestw-393 | 05H04 | Hemicolinium bromide | 0.84 | 0.99 |
| Prestw-394 | 05H05 | Kanamycin A sulfate | 0.97 | 1.05 |
| Prestw-395 | 05H06 | Amikacin hydrate | 0.95 | 0.98 |
| Prestw-396 | 05H07 | Etoposide | 0.97 | 1.04 |
| Code     | Reference  | Compound                      | Value1 | Value2 |
|----------|------------|-------------------------------|--------|--------|
| Prestw-397 | 05H08      | Clomiphene citrate (Z,E)     | 0.94   | 0.88   |
| Prestw-398 | 05H09      | Oxantel pamoate               | 0.93   | 1.03   |
| Prestw-399 | 05H10      | Prochlorperazine dimaleate    |        |        |
| Prestw-400 | 05H11      | Hesperid                      | 0.95   | 1.22   |
|           | Plate 6    |                               |        |        |
| Prestw-401 | 06A02      | Testosterone propionate       | 1.02   | 1.14   |
| Prestw-402 | 06A03      | Arecoline hydrobromide        | 1.03   | 1.12   |
| Prestw-403 | 06A04      | Thyroxine (L)                 | 1.00   | 0.87   |
| Prestw-1288 | 06A05     | Idebenone                     | 1.03   | 0.88   |
| Prestw-405 | 06A06      | Pepstatin A                   | 0.99   | 1.01   |
| Prestw-406 | 06A07      | SR-95639A                     | 0.99   | 1.06   |
| Prestw-407 | 06A08      | Adamantamine fumarate         | 1.03   | 1.20   |
| Prestw-408 | 06A09      | Butoconazole nitrate          | 1.04   | 1.38   |
| Prestw-409 | 06A10      | Amiodarone hydrochloride      | 1.00   | 1.34   |
| Prestw-410 | 06A11      | Amphotericin B                | 1.04   | 1.50   |
| Prestw-411 | 06B02      | Androsterone                  | 0.93   | 1.03   |
| Prestw-1489 | 06B03    | Amifostine                    | 0.94   | 1.09   |
| Prestw-413 | 06B04      | Carbarsone                    | 0.94   | 0.95   |
| Prestw-1219 | 06B05     | Amlodipine                    | 1.07   | 0.72   |
| Prestw-1147 | 06B06     | Modafinil                     | 1.00   | 0.99   |
| Prestw-416 | 06B07      | Bacampicillin hydrochloride   | 1.06   | 1.12   |
| Prestw-1298 | 06B08     | Lamivudine                    | 0.98   | 1.00   |
| Prestw-418 | 06B09      | Biotin                        | 0.99   | 1.27   |
| Code    | Compound                          | Min | Max |
|---------|-----------------------------------|-----|-----|
| Prestw-419 | Bisacodyl                         | 1.04| 1.28|
| Prestw-1242 | Erlotinib                         | 0.99| 1.25|
| Prestw-421 | Suloctidil                        | 0.99| 1.03|
| Prestw-1368 | Zotepine                          | 0.97| 0.82|
| Prestw-423 | Carisoprodol                      | 0.97| 1.02|
| Prestw-424 | Cephalosporanic acid, 7-amino    | 0.97| 1.07|
| Prestw-425 | Chicago sky blue 6B               | 0.88| 1.01|
| Prestw-426 | Buflomedil hydrochloride          | 0.98| 1.13|
| Prestw-1393 | Dibenzepine hydrochloride        | 1.06| 1.09|
| Prestw-428 | Roxatidine Acetate HCl            | 1.05| 1.26|
| Prestw-429 | Cholecalciferol                   | 1.00| 1.29|
| Prestw-430 | Cisapride                         | 0.97| 1.13|
| Prestw-1303 | Pefloxacin                      | 0.86| 1.05|
| Prestw-432 | Corticosterone                    | 1.03| 1.18|
| Prestw-433 | Cyanocobalamin                    | 0.85| 1.10|
| Prestw-434 | Cefadroxil                        | 0.94| 1.11|
| Prestw-435 | Cyclosporin A                     | 0.93| 0.45|
| Prestw-436 | Digitoxigenin                     | 1.12| 0.78|
| Prestw-437 | Digoxin                           | 1.11| 0.85|
| Prestw-438 | Doxorubicin hydrochloride         | 1.01| 1.06|
| Prestw-439 | Carbimazole                       | 0.95| 1.22|
| Prestw-440 | Epiandrosterone                   | 1.00| 1.23|
| Prestw-441 | Estradiol-17 beta                 | 0.88| 1.04|
| Code     | Code     | Name                                              | API      | AUC      |
|----------|----------|---------------------------------------------------|----------|----------|
| Prestw-1380 | 06E03    | Clobutinol hydrochloride                          | 0.98     | 1.22     |
| Prestw-443 | 06E04    | Gabazine                                          | 0.92     | 1.15     |
| Prestw-1156 | 06E05    | Oxcarbazepine                                     | 0.95     | 1.14     |
| Prestw-445 | 06E06    | Cyclobenzaprine hydrochloride                     | 0.96     | 0.87     |
| Prestw-446 | 06E07    | Carteolol hydrochloride                           | 0.98     | 1.11     |
| Prestw-447 | 06E08    | Hydrocortisone base                              | 1.06     | 1.22     |
| Prestw-448 | 06E09    | Hydroxytacrine maleate (R,S)                     | 1.02     | 1.31     |
| Prestw-449 | 06E10    | Pilocarpine nitrate                              | 1.02     | 1.33     |
| Prestw-450 | 06E11    | Dicloxacillin sodium salt                        | 1.03     | 1.18     |
| Prestw-451 | 06F02    | Alizapride HCl                                   | 1.00     | 1.20     |
| Prestw-1161 | 06F03   | Stanozolol                                       | 0.92     | 1.16     |
| Prestw-1257 | 06F04   | Calcipotriene                                    | 0.96     | 1.31     |
| Prestw-1429 | 06F05   | Linezolid                                        | 0.98     | 1.11     |
| Prestw-455 | 06F06    | Mebhydrolone 1,5-naphtalenedisulfonate            | 0.96     | 1.12     |
| Prestw-456 | 06F07    | Meclocycline sulfosalicylate                     | 0.98     | 1.06     |
| Prestw-457 | 06F08    | Meclozine dihydrochloride                        | 1.00     | 1.19     |
| Prestw-458 | 06F09    | Melatonin                                        | 0.98     | 1.25     |
| Prestw-1251 | 06F10   | Butalbital                                       | 1.08     | 1.43     |
| Prestw-460 | 06F11    | Dinoprost trometamol                             | 0.99     | 1.12     |
| Prestw-461 | 06G02    | Tropisetron HCl                                  | 0.98     | 1.11     |
| Prestw-462 | 06G03    | Cefixime                                         | 0.93     | 1.13     |
| Prestw-463 | 06G04    | Metrizamide                                      | 0.92     | 1.27     |
| Prestw-1323 | 06G05   | Quetiapine                                       | 0.80     | 1.04     |
| Code     | Section | Chemical Name                      | Ratio 1 | Ratio 2 |
|----------|---------|------------------------------------|---------|---------|
| Prestw-1464 | 06G06  | Tosufloxacin hydrochloride         | 0.93    | 1.13    |
| Prestw-1400 | 06G07  | Efavirenz                          | 0.81    | 1.01    |
| Prestw-1157 | 06G08  | Rifapentine                        | 0.96    | 1.13    |
| Prestw-468 | 06G09  | Neostigmine bromide                | 0.95    | 1.33    |
| Prestw-469 | 06G10  | Niridazole                         | 0.92    | 1.19    |
| Prestw-470 | 06G11  | Ceforanide                         | 0.90    | 1.12    |
| Prestw-1358 | 06H02  | Vatalanib                          | 0.79    | 0.99    |
| Prestw-1295 | 06H03  | Itopride                           | 0.89    | 1.03    |
| Prestw-473 | 06H04  | Cefotetan                          | 0.93    | 1.01    |
| Prestw-1254 | 06H05  | Fentiazac                          | 0.94    | 1.08    |
| Prestw-475 | 06H06  | Brompheniramine maleate            | 0.96    | 0.94    |
| Prestw-476 | 06H07  | Primaquine diphosphate             | 1.07    | 0.95    |
| Prestw-477 | 06H08  | Progesterone                       | 0.97    | 1.02    |
| Prestw-478 | 06H09  | Felodipine                         | 0.92    | 1.27    |
| Prestw-1325 | 06H10  | Raclopride                         | 0.96    | 1.23    |
| Prestw-1385 | 06H11  | Closantel                          | 0.97    | 1.41    |
| *Plate 7th* |         |                                    |         |         |
| Prestw-481  | 07A02  | Serotonin hydrochloride            | 0.78    | 1.33    |
| Prestw-482  | 07A03  | Cefotiam hydrochloride             | 0.90    | 1.05    |
| Prestw-1336 | 07A04  | Rofecoxib                          | 0.73    | 1.17    |
| Prestw-484  | 07A05  | Benperidol                         | 0.97    | 1.37    |
| Prestw-485  | 07A06  | Cefaclor                           | 0.89    | 1.20    |
| Prestw-486  | 07A07  | Colistin sulfate                   | 0.80    | 2.02    |
| Code     | Code     | Name                          | Value1 | Value2 |
|----------|----------|-------------------------------|--------|--------|
| Prestw-487 | 07A08    | Daunorubicin hydrochloride    | 0.87   | 1.02   |
| Prestw-488 | 07A09    | Dosulepin hydrochloride       | 0.90   | 1.09   |
| Prestw-489 | 07A10    | Ceftazidime pentahydrate      | 0.88   | 1.44   |
| Prestw-490 | 07A11    | Iobenguane sulfate            | 0.90   | 1.76   |
| Prestw-491 | 07B02    | Metixene hydrochloride        | 0.80   | 0.62   |
| Prestw-492 | 07B03    | Nitrofural                    | 0.87   | 1.29   |
| Prestw-493 | 07B04    | Omeprazole                    | 0.87   | 1.19   |
| Prestw-494 | 07B05    | Propylthiouracil              | 0.84   | 1.08   |
| Prestw-495 | 07B06    | Terconazole                   | 0.95   | 0.63   |
| Prestw-496 | 07B07    | Tiaprofenic acid              | 0.83   | 0.98   |
| Prestw-497 | 07B08    | Vancomycin hydrochloride      | 0.87   | 1.18   |
| Prestw-498 | 07B09    | Artemisinin                   | 0.89   | 1.32   |
| Prestw-499 | 07B10    | Propafenone hydrochloride     | 0.88   | 1.51   |
| Prestw-500 | 07B11    | Ethamivan                     | 0.79   | 1.81   |
| Prestw-501 | 07C02    | Vigabatrin                    | 0.81   | 1.46   |
| Prestw-502 | 07C03    | Biperiden hydrochloride       | 0.75   | 1.42   |
| Prestw-503 | 07C04    | Cetirizine dihydrochloride    | 0.70   | 1.45   |
| Prestw-504 | 07C05    | Etifenin                      | 0.91   | 1.18   |
| Prestw-505 | 07C06    | Metaproterenol sulfate, orciprenaline sulfate | 0.86 | 1.35 |
| Prestw-506 | 07C07    | Sisomicin sulfate             | 0.94   | 1.09   |
| Prestw-1159 | 07C08   | Sibutramine HCl               | 0.97   | 1.09   |
| Prestw-508 | 07C09    | Resveratrol                   | 0.80   | 0.91   |
| Prestw-509 | 07C10    | Bromperidol                   | 1.03   | 1.10   |
| Prestw-510 | 07C11 | Cyclizine hydrochloride | 0.88 | 1.17 |
| Prestw-511 | 07D02 | Fluoxetine hydrochloride | 0.87 | 1.27 |
| Prestw-512 | 07D03 | Iohexol | 0.92 | 1.45 |
| Prestw-513 | 07D04 | Norcyclobenzaprine | 0.89 | 1.02 |
| Prestw-514 | 07D05 | Pyrazinamide | 0.87 | 1.13 |
| Prestw-515 | 07D06 | Trimethadione | 0.96 | 1.24 |
| Prestw-516 | 07D07 | Lovastatin | 0.99 | 1.21 |
| Prestw-517 | 07D08 | Nystatine | 0.92 | 1.08 |
| Prestw-518 | 07D09 | Budesonide | 0.83 | 1.56 |
| Prestw-519 | 07D10 | Imipenem | 0.92 | 1.37 |
| Prestw-520 | 07D11 | Sulfasalazine | 0.57 | 0.90 |
| Prestw-1430 | 07E02 | Lofexidine | 0.99 | 1.31 |
| Prestw-522 | 07E03 | Thiostrepton | 0.84 | 1.40 |
| Prestw-1169 | 07E04 | Miglitol | 1.06 | 1.61 |
| Prestw-524 | 07E05 | Tiabendazole | 1.02 | 1.08 |
| Prestw-525 | 07E06 | Rifampicin | 0.87 | 1.19 |
| Prestw-526 | 07E07 | Ethionamide | 1.06 | 0.86 |
| Prestw-527 | 07E08 | Tenoxicam | 0.88 | 1.17 |
| Prestw-528 | 07E09 | Triflusal | 0.96 | 1.54 |
| Prestw-529 | 07E10 | Mesoridazine besylate | 0.96 | 1.23 |
| Prestw-530 | 07E11 | Trolox | 1.05 | 1.32 |
| Prestw-531 | 07F02 | Pirenperone | 0.99 | 1.54 |
| Prestw-532 | 07F03 | Isoquinoline, 6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydro, hydrochloride | 1.01 | 1.34 |
| Code   | Label                     | Value1 | Value2 |
|--------|---------------------------|--------|--------|
| Prestw-533 07F04 | Phenacetin                | 0.87   | 1.45   |
| Prestw-534 07F05 | Atovaquone                | 1.05   | 1.53   |
| Prestw-535 07F06 | Methoxamine hydrochloride | 1.02   | 1.29   |
| Prestw-953 07F07 | (S)-(-)-Atenolol          | 1.08   | 1.34   |
| Prestw-537 07F08 | Piracetam                 | 0.81   | 1.41   |
| Prestw-538 07F09 | Phenindione               | 1.08   | 1.50   |
| Prestw-539 07F10 | Thiocolchicoside          | 1.02   | 1.42   |
| Prestw-540 07F11 | Clorsulon                 | 0.98   | 1.44   |
| Prestw-541 07G02 | Ciclopirox ethanolamine   | 0.91   | 1.23   |
| Prestw-542 07G03 | Probenecid                | 0.92   | 1.28   |
| Prestw-543 07G04 | Betahistine mesylate      | 0.90   | 1.37   |
| Prestw-544 07G05 | Tobramycin                | 1.02   | 1.25   |
| Prestw-545 07G06 | Tetramisole hydrochloride | 0.87   | 1.16   |
| Prestw-546 07G07 | Pregnenolone              | 0.89   | 1.06   |
| Prestw-547 07G08 | Molsidomine               | 1.00   | 1.32   |
| Prestw-548 07G09 | Chloroquine diphosphate   | 1.10   | 1.20   |
| Prestw-549 07G10 | Trimetazidine dihydrochloride | 0.96 | 1.49   |
| Prestw-550 07G11 | Parthenolide              | 1.03   | 0.93   |
| Prestw-551 07H02 | Hexitetidine              | 0.83   | 1.27   |
| Prestw-552 07H03 | Selegiline hydrochloride  | 0.93   | 1.22   |
| Prestw-553 07H04 | Pentamidine isethionate   | 1.00   | 1.28   |
| Prestw-554 07H05 | Tolazamide                | 0.93   | 1.19   |
| Prestw-555 07H06 | Nifuroxazide              | 0.86   | 1.11   |
| Reference | Code     | Name                        | Ratio 1 | Ratio 2 |
|-----------|----------|-----------------------------|---------|---------|
| Prestw-1144 | 07H07   | Mirtazapine                 | 0.93    | 1.00    |
| Prestw-557 | 07H08   | Dirithromycin               | 0.88    | 1.03    |
| Prestw-558 | 07H09   | Gliclazide                  | 0.88    | 1.30    |
| Prestw-559 | 07H10   | DO 897/99                   | 0.96    | 1.28    |
| Prestw-560 | 07H11   | Prenylamine lactate         | 0.95    | 1.13    |
| **Plate 8** |         |                             |         |         |
| Prestw-1188 | 08A02  | Ziprasidone Hydrochloride   | 1.04    | 0.98    |
| Prestw-1441 | 08A03  | Mevastatin                  | 1.04    | 0.92    |
| Prestw-1322 | 08A04  | Pyridostigmine iodd         | 1.03    | 1.06    |
| Prestw-1491 | 08A05  | Pentobarbital               | 1.03    | 1.23    |
| Prestw-565 | 08A06   | Atropine sulfate monohydrate| 0.95    | 1.32    |
| Prestw-566 | 08A07   | Eserine sulfate, physostigmine sulfate | 1.03 | 1.02 |
| Prestw-1139 | 08A08  | Itraconazole                | 0.93    | 0.99    |
| Prestw-1174 | 08A09  | Acarbose                    | 0.98    | 1.48    |
| Prestw-1403 | 08A10  | Entacapone                  | 1.03    | 1.44    |
| Prestw-1449 | 08A11  | Nicotinamide                | 0.97    | 1.85    |
| Prestw-571 | 08B02   | Tetracaïne hydrochloride    | 0.99    | 1.22    |
| Prestw-572 | 08B03   | Mometasone furoate          | 1.07    | 1.17    |
| Prestw-1467 | 08B04  | Troglitazone                | 1.02    | 1.13    |
| Prestw-574 | 08B05   | Dacarbazine                 | 1.01    | 1.12    |
| Prestw-1351 | 08B06  | Tenatoprazole               | 0.99    | 1.15    |
| Prestw-576 | 08B07   | Acetopromazine maleate salt | 1.03 | 0.84 |
| Prestw-1271 | 08B08  | Escitalopram                | 0.91    | 0.89    |
| Code      | Page | Compound                        | C1 | C2 |
|-----------|------|---------------------------------|----|----|
| Prestw-1158 | 08B09 | Ropinirole HCl                  | 0.95 | 1.28 |
| Prestw-1297 | 08B10 | Lacidipine                      | 1.04 | 1.22 |
| Prestw-1228 | 08B11 | Argatroban                      | 0.93 | 1.46 |
| Prestw-1328 | 08C02 | Reboxetine mesylate             | 0.98 | 1.07 |
| Prestw-582  | 08C03 | Lobelanidine hydrochloride      | 0.95 | 1.26 |
| Prestw-583  | 08C04 | Papaverine hydrochloride        | 0.83 | 1.11 |
| Prestw-584  | 08C05 | Yohimbine hydrochloride         | 1.02 | 1.14 |
| Prestw-585  | 08C06 | Lobeline alpha (-) hydrochloride| 0.93 | 1.02 |
| Prestw-1211 | 08C07 | Alfacalcidol                    | 1.00 | 1.09 |
| Prestw-587  | 08C08 | Cilostazol                      | 0.97 | 0.99 |
| Prestw-588  | 08C09 | Galanthamine hydrobromide       | 0.98 | 1.13 |
| Prestw-1130 | 08C10 | Azelastine HCl                  | 0.95 | 1.04 |
| Prestw-1409 | 08C11 | Etretinate                      | 1.01 | 1.34 |
| Prestw-1274 | 08D02 | Emedastine                      | 1.09 | 1.28 |
| Prestw-1407 | 08D03 | Etofenamate                     | 0.81 | 1.28 |
| Prestw-1369 | 08D04 | Zaleplon                        | 0.96 | 1.24 |
| Prestw-594  | 08D05 | Diclofenac sodium               | 1.04 | 1.17 |
| Prestw-1410 | 08D06 | Exemestane                      | 0.93 | 1.09 |
| Prestw-596  | 08D07 | Convolamine hydrochloride       | 0.99 | 0.97 |
| Prestw-1183 | 08D08 | Temozolomide                    | 0.97 | 1.10 |
| Prestw-598  | 08D09 | Xylazine                        | 1.02 | 1.22 |
| Prestw-1132 | 08D10 | Celiprolol HCl                  | 1.00 | 1.11 |
| Prestw-1367 | 08D11 | Zopiclone                       | 0.97 | 1.18 |
| Code     | Description               | Min | Max |
|----------|---------------------------|-----|-----|
| Prestw- 1198 | Tranilast                | 0.91 | 1.16 |
| Prestw- 1182 | Tizanidine HCl           | 1.03 | 1.42 |
| Prestw- 1364 | Zafirlukast              | 0.94 | 1.54 |
| Prestw- 1252 | Butenafine               | 0.93 | 1.14 |
| Prestw- 1121 | Carbadox                 | 0.99 | 1.09 |
| Prestw- 1331 | Rimantadine              | 0.99 | 0.98 |
| Prestw- 607  | Eburnamonine (-)         | 0.96 | 1.22 |
| Prestw- 1460 | Oxibendazol              | 1.04 | 1.23 |
| Prestw- 1292 | Ipsapirone               | 0.96 | 1.29 |
| Prestw- 610  | Harmaline hydrochloride dihydrate | 0.97 | 1.11 |
| Prestw- 611  | Harmalol hydrochloride dihydrate | 0.94 | 1.23 |
| Prestw- 612  | Harmol hydrochloride monohydrate | 1.01 | 1.30 |
| Prestw- 613  | Harmine hydrochloride    | 0.88 | 1.10 |
| Prestw- 1177 | Carbidopa                | 0.93 | 1.08 |
| Prestw- 615  | Chrysene-1,4-quinone     | 1.00 | 1.06 |
| Prestw- 616  | Demecarium bromide       | 0.99 | 1.07 |
| Prestw- 617  | Quipazine dimaleate salt | 1.01 | 1.14 |
| Prestw- 1127 | Acipimox                 | 0.98 | 1.17 |
| Prestw- 619  | Diflorasone Diacetate    | 1.01 | 1.40 |
| Prestw- 620  | Harmane hydrochloride    | 0.98 | 1.22 |
| Prestw- 621  | Methoxy-6-harmalan       | 0.85 | 1.05 |
| Prestw- 1217 | Amisulpride              | 0.94 | 1.19 |
| Prestw- 623  | Pyridoxine hydrochloride | 0.93 | 1.23 |
| Code         | Component                          | 08G05 | 08G06 | 08G07 | 08G08 | 08G09 | 08G10 | 08G11 | 08H02 | 08H03 | 08H04 | 08H05 | 08H06 | 08H07 | 08H08 | 08H09 | 08H10 | 08H11 | 09A02 | 09A03 | 09A04 | 09A05 | 09A06 |
|-------------|------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Prestw-1469 | Mercaptopurine                     | 0.91  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1134 | Cytarabine                         | 0.91  | 0.90  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-626  | Racecadotril                       | 0.89  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-627  | Folic acid                         | 0.97  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1129 | Benazepril HCl                     | 0.92  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1178 | Aniracetam                         | 0.92  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-630  | Dimethisoquin hydrochloride        | 0.92  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1210 | Alendronate sodium                 | 0.91  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-632  | Dipivefrin hydrochloride           | 0.88  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-633  | Thiorphan                          | 0.88  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1463 | Tomoxetine hydrochloride           | 0.83  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1299 | Lapatinib ditosylate               | 0.94  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1488 | Penciclovir                        | 0.87  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1427 | Levetiracetam                      | 0.94  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1392 | Dexamfluramine hydrochloride       | 0.88  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1408 | Etoricoxib                         | 0.90  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1341 | Sertindole                         | 0.86  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Plate 9     | Sulmazole                          | 0.86  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-641  | Gefitinib                          | 0.87  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-1270 | Flunisolide                        | 0.93  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-643  | N-Acetyl-DL-homocysteine Thiolactone|       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-644  | Flurandrenolide                    | 0.89  |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Prestw-645  | Flurandrenolide                    |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Code   | Compound                           | Value1 | Value2 |
|--------|------------------------------------|--------|--------|
| Prestw-1125 | Oxiconazole Nitrate               | 0.89   | 0.87   |
| Prestw-1166 | Rebamipide                        | 0.89   | 1.02   |
| Prestw-1154 | Nilvadipine                       | 0.81   | 1.21   |
| Prestw-649 | Etanidazole                        | 0.81   | 1.24   |
| Prestw-650 | Butirosin disulfate salt           | 0.88   | 1.60   |
| Prestw-651 | Glimepiride                        | 0.82   | 0.94   |
| Prestw-652 | Picrotoxinin                       | 0.92   | 0.99   |
| Prestw-653 | Mepenzolate bromide               | 0.90   | 1.09   |
| Prestw-654 | Benfotamine                        | 0.87   | 1.00   |
| Prestw-655 | Halcinonide                        | 0.87   | 1.05   |
| Prestw-656 | Lanatoside C                       | 0.92   | 0.71   |
| Prestw-657 | Benzamil hydrochloride             | 0.93   | 0.78   |
| Prestw-658 | Suxibuzone                         | 0.84   | 1.20   |
| Prestw-659 | 6-Furfurylaminopurine              | 0.87   | 1.10   |
| Prestw-660 | Avermectin B1a                     | 0.85   | 1.16   |
| Prestw-1317 | Pranlukast                         | 0.88   | 0.97   |
| Prestw-1477 | Penicillamine                      | 0.91   | 1.12   |
| Prestw-1365 | Zileuton                           | 0.91   | 0.98   |
| Prestw-1432 | Loratadine                         | 0.85   | 0.96   |
| Prestw-1201 | Clindamycin Phosphate             | 0.89   | 1.06   |
| Prestw-666 | Nisoldipine                        | 0.84   | 0.84   |
| Prestw-667 | Foliosidine                        | 0.92   | 0.83   |
| Prestw-1165 | Acitretin                          | 0.87   | 1.08   |
| Code       | Code       | Chemical Name                        | C1    | C2    |
|------------|------------|--------------------------------------|-------|-------|
| Prestw-1162| 09C10      | Zonisamide                           | 0.95  | 1.27  |
| Prestw-1173| 09C11      | Irsogladine Maleate                  | 0.90  | 1.06  |
| Prestw-671 | 09D02      | Dydrogesterone                       | 0.93  | 1.19  |
| Prestw-1346| 09D03      | Sumatriptan succinate                | 0.88  | 1.21  |
| Prestw-1456| 09D04      | Opipramol dihydrochloride            | 0.82  | 0.86  |
| Prestw-1447| 09D05      | Nalidixic acid sodium salt           | 0.94  | 1.05  |
| Prestw-1475| 09D06      | Oxacillin Na                         | 0.96  | 1.05  |
| Prestw-676 | 09D07      | Beta-Escin                           | 0.91  | 0.97  |
| Prestw-1496| 09D08      | Tiludronate disodium                 | 0.91  | 0.90  |
| Prestw-1349| 09D09      | Tazobactam                           | 0.87  | 1.15  |
| Prestw-1285| 09D10      | Ibandronate                          | 0.93  | 1.02  |
| Prestw-1363| 09D11      | Warfarin                             | 0.98  | 1.16  |
| Prestw-1318| 09E02      | Pranoprofen                          | 0.91  | 1.14  |
| Prestw-1340| 09E03      | Secnidazole                          | 0.93  | 1.21  |
| Prestw-683 | 09E04      | Pempidine tartrate                   | 0.97  | 1.33  |
| Prestw-1381| 09E05      | Clodronate                           | 0.92  | 1.14  |
| Prestw-685 | 09E06      | Nitrarine dihydrochloride            | 0.98  | 0.83  |
| Prestw-1194| 09E07      | Thimerosal                           | 0.95  | 0.25  |
| Prestw-1465| 09E08      | Tramadol hydrochloride               | 0.96  | 0.97  |
| Prestw-688 | 09E09      | Estropipate                          | 0.96  | 1.04  |
| Prestw-1253| 09E10      | Butylscopolammonium (n-) bromide     | 0.93  | 1.08  |
| Prestw-1494| 09E11      | Irinotecan Hydrochloride             | 0.94  | 1.02  |
| Prestw-1353| 09F02      | Tylosin                              | 1.00  | 1.09  |
| Code   | Value | Description                               | Mean | SD  |
|--------|-------|-------------------------------------------|------|-----|
| 09F03  | 0.96  | Citalopram Hydrobromide                   |      |     |
| 09F04  | 0.99  | Promazine hydrochloride                   |      |     |
| 09F05  | 0.97  | Sulfamerazine                              |      |     |
| 09F06  | 1.03  | Venlafaxine                               |      |     |
| 09F07  | 1.01  | Ethotoin                                  |      |     |
| 09F08  | 0.91  | 3-alpha-Hydroxy-5-beta-androstan-17-one   |      |     |
| 09F09  | 0.96  | Tetrahydrozoline hydrochloride            |      |     |
| 09F10  | 1.00  | Hexestrol                                 |      |     |
| 09F11  | 0.96  | Cefmetazole sodium salt                   |      |     |
| 09G02  | 0.91  | Trihexyphenidyl-D,L Hydrochloride         |      |     |
| 09G03  | 0.88  | Succinylsulfathiazole                     |      |     |
| 09G04  | 0.86  | Famprofazone                              |      |     |
| 09G05  | 1.03  | Bromopride                                |      |     |
| 09G06  | 1.32  | Methyl benzethonium chloride              |      |     |
| 09G07  | 0.77  | Chlorcyclizine hydrochloride              |      |     |
| 09G08  | 0.88  | Diphenylpyraline hydrochloride            |      |     |
| 09G09  | 1.09  | Benzethonium chloride                     |      |     |
| 09G10  | 0.96  | Trioxsalen                                |      |     |
| 09G11  | 0.93  | Doxofylline                               |      |     |
| 09H02  | 0.88  | Sulfabenzamide                            |      |     |
| 09H03  | 0.87  | Benzocaine                                |      |     |
| 09H04  | 0.92  | Dipyrone                                  |      |     |
| 09H05  | 0.90  | Isosorbide dinitrate                      |      |     |
| Code     | Description                  | 09H06 | 09H07 | 09H08 | 09H09 | 09H10 | 09H11 |
|----------|------------------------------|------|------|------|------|------|------|
| Prestw-715 | Sulfachloropyridazine      | 0.85 | 0.88 |      |      |      |      |
| Prestw-716 | Pramoxine hydrochloride    | 0.94 | 1.01 |      |      |      |      |
| Prestw-717 | Finasteride                 | 0.88 | 0.97 |      |      |      |      |
| Prestw-718 | Fluorometholone             | 0.88 | 1.08 |      |      |      |      |
| Prestw-719 | Cephalothin sodium salt     | 0.88 | 1.08 |      |      |      |      |
| Prestw-720 | Cefuroxime sodium salt      | 0.90 | 1.11 |      |      |      |      |
| Plate 10  |                              |      |      |      |      |      |      |
| Prestw-721 | Althiazide                  | 1.01 | 0.97 |      |      |      |      |
| Prestw-722 | Isopyrin hydrochloride      | 1.02 | 0.99 |      |      |      |      |
| Prestw-723 | Phenethicillin potassium salt | 1.01 | 0.97 |      |      |      |      |
| Prestw-724 | Sulfamethoxypyridazine      | 0.95 | 0.87 |      |      |      |      |
| Prestw-725 | Deferoxamine mesylate       | 0.96 | 0.91 |      |      |      |      |
| Prestw-726 | Mephentermine hemisulfate   | 0.83 | 0.96 |      |      |      |      |
| Prestw-727 | Liranaftate                 | 0.93 | 0.99 |      |      |      |      |
| Prestw-728 | Sulfadimethoxine            | 0.89 | 0.88 |      |      |      |      |
| Prestw-729 | Sulfanilamide               | 0.80 | 0.94 |      |      |      |      |
| Prestw-730 | Balsalazide Sodium          | 0.84 | 0.95 |      |      |      |      |
| Prestw-731 | Sulfadinoxaline sodium salt | 0.94 | 1.00 |      |      |      |      |
| Prestw-732 | Streptozotocin              | 0.99 | 1.09 |      |      |      |      |
| Prestw-733 | Metoprolol-(+,-) (+)-tartrate salt | 1.01 | 1.04 |      |      |      |      |
| Prestw-734 | Flumethasone                | 0.92 | 1.08 |      |      |      |      |
| Prestw-735 | Flecainide acetate          | 0.99 | 1.02 |      |      |      |      |
| Prestw-736 | Cefazolin sodium salt       | 0.92 | 1.04 |      |      |      |      |
| Code     | Code-1  | Chemical Name                     | Value 1 | Value 2 |
|----------|---------|-----------------------------------|---------|---------|
| Prestw-737 | 10B08   | Atractyloside potassium salt      | 0.90    | 1.11    |
| Prestw-738 | 10B09   | Folinic acid calcium salt         | 0.92    | 0.99    |
| Prestw-739 | 10B10   | Levonordefrin                     | 0.90    | 1.02    |
| Prestw-740 | 10B11   | Ebselen                           | 0.91    | 1.15    |
| Prestw-741 | 10C02   | Nadide                            | 0.89    | 1.11    |
| Prestw-742 | 10C03   | Sulfamethizole                    | 0.93    | 1.09    |
| Prestw-743 | 10C04   | Medrysone                         | 0.93    | 1.03    |
| Prestw-744 | 10C05   | Flunixin meglumine                | 0.92    | 1.02    |
| Prestw-745 | 10C06   | Spiramycin                        | 0.98    | 1.08    |
| Prestw-746 | 10C07   | Glycopyrrolate                    | 1.01    | 1.09    |
| Prestw-747 | 10C08   | Cefamandole sodium salt           | 0.90    | 1.02    |
| Prestw-748 | 10C09   | Monensin sodium salt              | 0.97    | 1.19    |
| Prestw-749 | 10C10   | Isoetharine mesylate salt         | 0.85    | 1.03    |
| Prestw-750 | 10C11   | Mevalonic-D, L acid lactone       | 0.91    | 1.08    |
| Prestw-751 | 10D02   | Terazosin hydrochloride           | 0.87    | 1.10    |
| Prestw-752 | 10D03   | Phenazopyridine hydrochloride     | 0.86    | 1.05    |
| Prestw-753 | 10D04   | Demeclocycline hydrochloride      | 0.90    | 1.00    |
| Prestw-754 | 10D05   | Fenoprofen calcium salt dihydrate | 0.93    | 1.05    |
| Prestw-755 | 10D06   | Piperacillin sodium salt          | 0.95    | 1.11    |
| Prestw-756 | 10D07   | Diethylstilbestrol                | 0.90    | 1.01    |
| Prestw-757 | 10D08   | Chlorotrianisene                  | 0.90    | 1.04    |
| Prestw-758 | 10D09   | Ribostamycin sulfate salt         | 0.88    | 0.95    |
| Prestw-759 | 10D10   | Methacholine chloride             | 0.93    | 0.94    |
| Code   | Compound                        | Value1 | Value2 |
|--------|---------------------------------|--------|--------|
| Prestw-760 | 10D11 Pipenzolate bromide     | 0.81   | 0.96   |
| Prestw-761 | 10E02 Butamben                | 0.87   | 1.08   |
| Prestw-762 | 10E03 Sulfapyridine           | 0.89   | 0.98   |
| Prestw-763 | 10E04 Meclofenoxate hydrochloride | 0.92 | 1.14   |
| Prestw-764 | 10E05 Furaladone hydrochloride | 0.92   | 0.96   |
| Prestw-765 | 10E06 Ethoxyquin              | 0.83   | 0.92   |
| Prestw-766 | 10E07 Tinidazole              | 0.91   | 1.06   |
| Prestw-767 | 10E08 Guanadrel sulfate       | 0.88   | 0.96   |
| Prestw-768 | 10E09 Vidarabine              | 0.91   | 1.01   |
| Prestw-769 | 10E10 Sulfameter              | 0.86   | 0.88   |
| Prestw-770 | 10E11 Isopropamide iodide     | 0.88   | 0.96   |
| Prestw-771 | 10F02 Alclometasone dipropionate | 0.85 | 1.15   |
| Prestw-772 | 10F03 Leflunomide             | 0.85   | 0.94   |
| Prestw-773 | 10F04 Norgestrel-(D)         | 0.85   | 0.96   |
| Prestw-774 | 10F05 Fluocinonide            | 0.91   | 1.14   |
| Prestw-775 | 10F06 Sulfamethazine sodium salt | 0.88 | 1.06   |
| Prestw-776 | 10F07 Guaifenesin           | 0.96   | 1.04   |
| Prestw-777 | 10F08 Alexidine dihydrochloride | 16.01 | 6.74   |
| Prestw-778 | 10F09 Proadifen hydrochloride | 0.81   | 0.95   |
| Prestw-779 | 10F10 Zomepirac sodium salt   | 0.81   | 0.95   |
| Prestw-780 | 10F11 Cinoxacin               | 0.79   | 1.02   |
| Prestw-781 | 10G02 Clobetasol propionate   | 0.85   | 1.02   |
| Prestw-782 | 10G03 Podophyllotoxin         | 0.94   | 0.68   |
| Code     | Description                        | Value1 | Value2 |
|----------|------------------------------------|--------|--------|
| Prestw-783 | Clofibric acid                        | 0.84   | 1.03   |
| Prestw-784 | Bendroflumethiazide                 | 0.88   | 1.04   |
| Prestw-785 | Dicumarol                           | 0.91   | 1.11   |
| Prestw-786 | Methimazole                         | 0.84   | 0.93   |
| Prestw-787 | Merbromin                           | 0.74   | 0.89   |
| Prestw-788 | Hexylcaine hydrochloride            | 0.81   | 1.00   |
| Prestw-789 | Drofenine hydrochloride             | 0.78   | 0.97   |
| Prestw-790 | Cycloheximide                       | 0.80   | 0.99   |
| Prestw-791 | (R) -Naproxen sodium salt           | 0.77   | 0.93   |
| Prestw-792 | Propidium iodide                    | 0.74   | 0.85   |
| Prestw-793 | Cloperastine hydrochloride          | 0.82   | 0.80   |
| Prestw-794 | Eucatropine hydrochloride           | 0.80   | 0.82   |
| Prestw-795 | Isocarboxazid                       | 0.83   | 0.79   |
| Prestw-796 | Lithocholic acid                    | 0.78   | 0.78   |
| Prestw-797 | Methotrimeprazine maleat salt       | 0.84   | 0.81   |
| Prestw-798 | Dienestrol                          | 0.84   | 0.86   |
| Prestw-799 | Pridinol methanesulfonate salt      | 0.78   | 0.95   |
| Prestw-800 | Amrinone                            | 0.77   | 0.96   |
| Plate 11  |                                    |        |        |
| Prestw-801 | Carbinoxamine maleate salt          | 0.91   | 1.04   |
| Prestw-802 | Methazolamide                       | 0.99   | 1.00   |
| Prestw-803 | Pyrithyldione                       | 1.01   | 1.12   |
| Prestw-804 | Spectinomycbin dihydrochloride      | 0.99   | 0.99   |
| Prestw-805 | 11A06  | Piromidic acid | 1.01  | 1.09  |
| Prestw-806 | 11A07  | Trimipramine maleate salt | 0.91  | 0.95  |
| Prestw-807 | 11A08  | Chloropyramine hydrochloride | 0.95  | 1.04  |
| Prestw-808 | 11A09  | Furazolidone | 0.97  | 1.12  |
| Prestw-809 | 11A10  | Dichlorphenamide | 0.92  | 1.26  |
| Prestw-810 | 11A11  | Sulconazole nitrate | 1.02  | 1.18  |
| Prestw-1233 | 11B02  | Auranofin | 1.02  | 0.49  |
| Prestw-812 | 11B03  | Cromolyn disodium salt | 0.98  | 0.87  |
| Prestw-813 | 11B04  | Bucladesine sodium salt | 0.94  | 0.88  |
| Prestw-814 | 11B05  | Cefsulodin sodium salt | 0.96  | 0.84  |
| Prestw-815 | 11B06  | Fosfosal | 0.96  | 1.10  |
| Prestw-816 | 11B07  | Suprofen | 0.92  | 1.03  |
| Prestw-817 | 11B08  | Catechin- (+,-) hydrate | 0.92  | 1.08  |
| Prestw-818 | 11B09  | Nadolol | 0.94  | 1.19  |
| Prestw-819 | 11B10  | Moxalactam disodium salt | 1.03  | 1.16  |
| Prestw-820 | 11B11  | Aminophylline | 0.97  | 0.99  |
| Prestw-821 | 11C02  | Azlocillin sodium salt | 0.98  | 1.07  |
| Prestw-822 | 11C03  | Clidinium bromide | 0.94  | 0.96  |
| Prestw-823 | 11C04  | Sulfamonomethoxine | 0.99  | 0.99  |
| Prestw-824 | 11C05  | Benzthiazide | 1.01  | 1.03  |
| Prestw-825 | 11C06  | Trichlormethiazide | 0.97  | 1.23  |
| Prestw-826 | 11C07  | Oxalamine citrate salt | 0.92  | 1.18  |
| Prestw-827 | 11C08  | Propantheline bromide | 0.94  | 1.19  |
| Code | Code | Name                                           | 1   | 2    |
|------|------|------------------------------------------------|-----|------|
| Prestw-1361 | 11C09 | Viloxazine hydrochloride                        | 0.98| 0.99 |
| Prestw-829   | 11C10 | Dimethadione                                    | 0.92| 1.01 |
| Prestw-830   | 11C11 | Ethaverine hydrochloride                        | 0.89| 0.93 |
| Prestw-831   | 11D02 | Butacaine                                       | 0.93| 0.97 |
| Prestw-832   | 11D03 | Cefoxitin sodium salt                           | 0.96| 0.99 |
| Prestw-833   | 11D04 | Ifosfamide                                      | 0.95| 1.11 |
| Prestw-834   | 11D05 | Novobiocin sodium salt                          | 0.85| 1.09 |
| Prestw-835   | 11D06 | Tetrahydroxy-1,4-quinone monohydrate            | 1.03| 1.19 |
| Prestw-836   | 11D07 | Indoprofen                                      | 0.83| 1.26 |
| Prestw-837   | 11D08 | Carbenoxolone disodium salt                     | 0.90| 1.01 |
| Prestw-838   | 11D09 | Iocetamic acid                                  | 0.93| 1.13 |
| Prestw-839   | 11D10 | Ganciclovir                                     | 0.89| 1.20 |
| Prestw-840   | 11D11 | Ethopropazine hydrochloride                     | 0.94| 0.78 |
| Prestw-1455  | 11E02 | Olanzapine                                      | 0.95| 0.88 |
| Prestw-842   | 11E03 | Trimeprazine tartrate                           | 0.85| 0.63 |
| Prestw-843   | 11E04 | Nafcillin sodium salt monohydrate               | 0.85| 1.07 |
| Prestw-844   | 11E05 | Procyclidine hydrochloride                      | 0.86| 0.95 |
| Prestw-845   | 11E06 | Amiprilose hydrochloride                        | 0.92| 1.10 |
| Prestw-846   | 11E07 | Ethynylestradiol 3-methyl ether                 | 0.97| 1.05 |
| Prestw-847   | 11E08 | (-) -Levobunolol hydrochloride                  | 0.91| 1.06 |
| Prestw-848   | 11E09 | Iodixanol                                       | 0.90| 1.10 |
| Prestw-849   | 11E10 | Rolitetracycline                                | 0.78| 0.97 |
| Prestw-850   | 11E11 | Equilin                                         | 0.90| 0.87 |
|   |   |   |   |   |
|---|---|---|---|---|
| Prestw-851 | 11F02 | Paroxetine Hydrochloride | 0.95 | 0.78 |
| Prestw-1454 | 11F03 | Nylidrin | 0.89 | 0.91 |
| Prestw-853 | 11F04 | Liothyronine | 0.87 | 1.07 |
| Prestw-854 | 11F05 | Roxithromycin | 0.91 | 1.01 |
| Prestw-855 | 11F06 | Beclomethasone dipropionate | 0.89 | 1.16 |
| Prestw-856 | 11F07 | Tolmetin sodium salt dihydrate | 0.97 | 1.11 |
| Prestw-857 | 11F08 | (+) -Levobunolol hydrochloride | 0.97 | 1.10 |
| Prestw-858 | 11F09 | Doxazosin mesylate | 0.87 | 0.92 |
| Prestw-859 | 11F10 | Fluvastatin sodium salt | 0.88 | 0.98 |
| Prestw-860 | 11F11 | Methylhydantoin-5-(L) | 0.91 | 0.87 |
| Prestw-861 | 11G02 | Gabapentin | 0.84 | 0.94 |
| Prestw-862 | 11G03 | Raloxifene hydrochloride | 0.89 | 0.82 |
| Prestw-863 | 11G04 | Etidronic acid, disodium salt | 0.92 | 0.91 |
| Prestw-864 | 11G05 | Methylhydantoin-5-(D) | 0.88 | 1.04 |
| Prestw-865 | 11G06 | Simvastatin | 0.88 | 0.94 |
| Prestw-866 | 11G07 | Azacytidine-5 | 0.86 | 0.91 |
| Prestw-867 | 11G08 | Paromomycin sulfate | 0.83 | 1.10 |
| Prestw-868 | 11G09 | Acetaminophen | 0.89 | 1.04 |
| Prestw-869 | 11G10 | Phthalylsulfathiazole | 0.87 | 0.97 |
| Prestw-870 | 11G11 | Luteolin | 0.81 | 0.96 |
| Prestw-871 | 11H02 | Iopamidol | 0.88 | 1.11 |
| Prestw-872 | 11H03 | Iopromide | 0.82 | 1.10 |
| Prestw-873 | 11H04 | Theophylline monohydrate | 0.86 | 0.94 |
| Code     | Plate | Name                               | Value1 | Value2 |
|----------|-------|------------------------------------|--------|--------|
| Prestw-874 | 11H05 | Theobromine                        | 0.90   | 0.97   |
| Prestw-875 | 11H06 | Reserpine                          | 0.81   | 0.76   |
| Prestw-1239 | 11H07 | Bicalutamide                       | 0.84   | 0.90   |
| Prestw-877 | 11H08 | Scopolamine hydrochloride          | 0.88   | 0.89   |
| Prestw-878 | 11H09 | Ioversol                           | 0.84   | 0.96   |
| Prestw-1495 | 11H10 | Rabeprazole                        | 0.79   | 0.93   |
| Prestw-880 | 11H11 | Carbachol                          | 0.91   | 0.97   |
| Plate 12 |       |                                    |        |        |
| Prestw-881 | 12A02 | Niacin                             | 1.03   | 1.17   |
| Prestw-882 | 12A03 | Bemegride                          | 1.04   | 1.14   |
| Prestw-883 | 12A04 | Digoxigenin                        | 1.03   | 0.86   |
| Prestw-884 | 12A05 | Meglumine                          | 0.98   | 1.11   |
| Prestw-885 | 12A06 | Cantharidin                        | 0.98   | 1.03   |
| Prestw-886 | 12A07 | Clioquinol                         | 0.93   | 1.18   |
| Prestw-887 | 12A08 | Oxybenzone                         | 0.94   | 1.14   |
| Prestw-888 | 12A09 | Promethazine hydrochloride         | 0.89   | 1.03   |
| Prestw-1167 | 12A10 | Diacerein                          | 0.94   | 1.06   |
| Prestw-1137 | 12A11 | Esmolol hydrochloride              | 0.90   | 1.13   |
| Prestw-1486 | 12B02 | Cortisol acetate                   | 0.97   | 0.93   |
| Prestw-1416 | 12B03 | Flubendazol                        | 0.97   | 0.95   |
| Prestw-893  | 12B04 | Felbinac                           | 1.00   | 0.88   |
| Prestw-894  | 12B05 | Butylparaben                       | 1.03   | 0.86   |
| Prestw-895  | 12B06 | Aminohippuric acid                 | 0.91   | 0.90   |
| Code   | Compound                          | Value1 | Value2 |
|--------|-----------------------------------|--------|--------|
| Prestw-896 | 12B07 N-Acetyl-L-leucine           | 1.02   | 0.92   |
| Prestw-897 | 12B08 Pipemidic acid              | 0.98   | 0.95   |
| Prestw-898 | 12B09 Dioxybenzone                | 0.95   | 0.79   |
| Prestw-899 | 12B10 Adrenosterone               | 0.99   | 0.75   |
| Prestw-900 | 12B11 Methylatropine nitrate      | 1.00   | 0.98   |
| Prestw-901 | 12C02 Hymecromone                | 0.96   | 0.97   |
| Prestw-902 | 12C03 Caffeic acid               | 0.90   | 0.94   |
| Prestw-903 | 12C04 Diloxanide furoate         | 0.95   | 0.94   |
| Prestw-904 | 12C05 Metyrapone                 | 0.93   | 0.91   |
| Prestw-905 | 12C06 Urapidil hydrochloride     | 0.96   | 0.89   |
| Prestw-906 | 12C07 Fluspirilen                | 0.95   | 0.78   |
| Prestw-907 | 12C08 S-(+)-ibuprofen            | 1.00   | 0.86   |
| Prestw-908 | 12C09 Ethynodiol diacetate       | 0.99   | 0.82   |
| Prestw-909 | 12C10 Nabumetone                 | 0.96   | 0.74   |
| Prestw-910 | 12C11 Nisoxetine hydrochloride  | 0.96   | 0.83   |
| Prestw-911 | 12D02 (+)-Isoproterenol (+)-bitartrate salt | 0.98 | 0.88 |
| Prestw-912 | 12D03 Monobenzone                | 0.90   | 0.82   |
| Prestw-913 | 12D04 2-Aminobenzenesulfonamide  | 0.92   | 1.12   |
| Prestw-914 | 12D05 Estrone                    | 1.01   | 1.20   |
| Prestw-915 | 12D06 Lorglumide sodium salt     | 0.83   | 1.16   |
| Prestw-916 | 12D07 Nitrendipine               | 0.82   | 0.67   |
| Prestw-917 | 12D08 Flurbiprofen               | 0.82   | 0.87   |
| Prestw-918 | 12D09 Nimodipine                 | 0.87   | 0.81   |
| Code   | Description                        | Value 1       | Value 2       |
|--------|------------------------------------|---------------|---------------|
| Prestw-919 |                       | 12D10   | Bacitracin                  | 0.95 | 0.93|
| Prestw-920 |                        | 12D11   | L(-)-vesamicol hydrochloride | 0.91 | 0.86|
| Prestw-921 |                        | 12E02   | Nizatididine              | 0.91 | 0.96|
| Prestw-922 |                        | 12E03   | Thioperamide maleate       | 0.87 | 0.89|
| Prestw-923 |                        | 12E04   | Xamoterol hemifumarate     | 0.89 | 0.91|
| Prestw-924 |                        | 12E05   | Rolipram                  | 0.99 | 0.97|
| Prestw-925 |                        | 12E06   | Thonzonium bromide         | 1.36 | 0.89|
| Prestw-926 |                        | 12E07   | Idazoxan hydrochloride     | 0.97 | 0.84|
| Prestw-927 |                        | 12E08   | Quinapril HCl              | 0.92 | 0.83|
| Prestw-928 |                        | 12E09   | Nilutamide                 | 0.91 | 0.90|
| Prestw-929 |                        | 12E10   | Ketorolac tromethamine     | 0.87 | 0.85|
| Prestw-930 |                        | 12E11   | Protriptyline hydrochloride | 0.89 | 0.76|
| Prestw-931 |                        | 12F02   | Propofol                   | 0.87 | 0.94|
| Prestw-932 |                        | 12F03   | S(-)Eticlopride hydrochloride | 0.97 | 0.89|
| Prestw-933 |                        | 12F04   | Primidone                  | 0.93 | 0.99|
| Prestw-934 |                        | 12F05   | Flucytosine                | 0.91 | 1.04|
| Prestw-935 |                        | 12F06   | (-)-MK 801 hydrogen maleate | 0.86 | 1.02|
| Prestw-936 |                        | 12F07   | Bephenium hydroxynaphthoate | 0.97 | 0.86|
| Prestw-937 |                        | 12F08   | Dehydroisoandrosterone 3-acetate | 0.90 | 0.90|
| Prestw-938 |                        | 12F09   | Benserazide hydrochloride  | 0.91 | 0.84|
| Prestw-939 |                        | 12F10   | Iodipamide                 | 0.94 | 0.84|
| Prestw-1213 |                       | 12F11   | Allopurinol               | 0.95 | 0.81|
| Prestw-941 |                        | 12G02   | Pentetic acid              | 0.91 | 1.00|
| Code     | Description                                      | Value 1 | Value 2 |
|----------|--------------------------------------------------|---------|---------|
| Prestw-942 | 12G03  Bretylium tosylate                       | 0.88    | 0.95    |
| Prestw-943 | 12G04  Pralidoxime chloride                     | 0.85    | 0.93    |
| Prestw-944 | 12G05  Phenoxybenzamine hydrochloride           | 0.88    | 0.93    |
| Prestw-945 | 12G06  Salmeterol                               | 0.86    | 0.80    |
| Prestw-946 | 12G07  Altretamine                              | 0.88    | 0.83    |
| Prestw-947 | 12G08  Prazosin hydrochloride                   | 0.90    | 0.78    |
| Prestw-948 | 12G09  Timolol maleate salt                    | 0.96    | 0.84    |
| Prestw-949 | 12G10  (+,-)-Octopamine hydrochloride          | 0.89    | 0.80    |
| Prestw-1279 | 12G11  Stavudine                               | 0.92    | 0.89    |
| Prestw-951 | 12H02  Crotamiton                               | 0.82    | 0.99    |
| Prestw-1197 | 12H03  Toremifene                             | 0.85    | 0.87    |
| Prestw-536 | 12H04  (R)-(+) - Atenolol                      | 0.86    | 1.03    |
| Prestw-954 | 12H05  Tyloxapol                                | 0.88    | 1.03    |
| Prestw-955 | 12H06  Florfenicol                             | 0.87    | 0.95    |
| Prestw-956 | 12H07  Megestrol acetate                       | 0.88    | 1.00    |
| Prestw-957 | 12H08  Deoxycorticosterone                    | 0.83    | 0.93    |
| Prestw-958 | 12H09  Urosiol                                 | 0.94    | 0.98    |
| Prestw-959 | 12H10  Proparacaine hydrochloride              | 0.85    | 1.03    |
| Prestw-960 | 12H11  Aminocaproic acid                       | 0.90    | 0.84    |
| **Plate 13** |                                          |         |         |
| Prestw-961 | 13A02  Denatonium benzoate                     | 1.01    | 1.02    |
| Prestw-1259 | 13A03  Canrenone                              | 1.04    | 1.03    |
| Prestw-963 | 13A04  Enilconazole                           | 1.02    | 1.08    |
| Code     | Code     | Compound                                 | Min | Max |
|----------|----------|------------------------------------------|-----|-----|
| Prestw-964 | 13A05    | Methacycline hydrochloride               | 0.98| 1.03|
| Prestw-1415 | 13A06    | Floxuridine                               | 1.06| 1.26|
| Prestw-966 | 13A07    | Sotalol hydrochloride                     | 0.98| 1.26|
| Prestw-1267 | 13A08    | Gestrinone                                | 1.01| 1.18|
| Prestw-968 | 13A09    | Decamethonium bromide                     | 1.01| 1.26|
| Prestw-969 | 13A10    | 3-Acetamidocoumarin                      | 0.98| 1.26|
| Prestw-970 | 13A11    | Roxarsone                                 | 0.92| 1.21|
| Prestw-971 | 13B02    | Remoxipride Hydrochloride                 | 0.94| 0.95|
| Prestw-972 | 13B03    | THIP Hydrochloride                        | 1.01| 0.98|
| Prestw-973 | 13B04    | Pirilindole mesylate                      | 0.96| 0.97|
| Prestw-974 | 13B05    | Pronethalol hydrochloride                 | 0.95| 1.05|
| Prestw-975 | 13B06    | Naftopidil dihydrochloride                | 0.96| 1.06|
| Prestw-976 | 13B07    | Tracazolate hydrochloride                 | 0.97| 1.04|
| Prestw-977 | 13B08    | Zardaverine                               | 1.02| 1.19|
| Prestw-978 | 13B09    | Memantine Hydrochloride                   | 0.96| 1.29|
| Prestw-979 | 13B10    | Ozagrel hydrochloride                     | 1.00| 1.10|
| Prestw-980 | 13B11    | Piribedil hydrochloride                   | 1.02| 1.20|
| Prestw-981 | 13C02    | Nitrocarbamphen hydrochloride             | 0.91| 0.97|
| Prestw-982 | 13C03    | Nandrolone                                | 1.00| 1.00|
| Prestw-983 | 13C04    | Dimaprit dihydrochloride                  | 0.99| 1.08|
| Prestw-1459 | 13C05    | Oxfendazol                                | 1.03| 1.05|
| Prestw-1268 | 13C06    | Guaiacol                                  | 0.92| 1.19|
| Prestw-986 | 13C07    | Proscillaridin A                          | 0.97| 0.76|
|     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|
| Prestw-1316 | 13C08 | Pramipexole | 0.97 | 1.21 |
| Prestw-1452 | 13C09 | Norgestimate | 1.05 | 1.09 |
| Prestw-1374 | 13C10 | Chlormadinone acetate | 0.95 | 1.21 |
| Prestw-1310 | 13C11 | Phenylbutazone | 0.93 | 1.25 |
| Prestw-991 | 13D02 | Gliquidone | 0.90 | 1.04 |
| Prestw-992 | 13D03 | Pizotifen malate | 0.92 | 0.82 |
| Prestw-993 | 13D04 | Ribavirin | 0.95 | 1.10 |
| Prestw-994 | 13D05 | Cyclpenthiazide | 0.95 | 1.10 |
| Prestw-995 | 13D06 | Fluvoxamine maleate | 0.90 | 1.21 |
| Prestw-1321 | 13D07 | Prothionamide | 0.99 | 1.06 |
| Prestw-997 | 13D08 | Fluticasone propionate | 0.93 | 1.20 |
| Prestw-998 | 13D09 | Zuclopenthixol hydrochloride | 0.97 | 0.60 |
| Prestw-999 | 13D10 | Proguanil hydrochloride | 0.87 | 1.14 |
| Prestw-1000 | 13D11 | Lymecycline | 0.91 | 1.16 |
| Prestw-1001 | 13E02 | Alfadolone acetate | 0.92 | 1.36 |
| Prestw-1002 | 13E03 | Alfaxalone | 1.01 | 1.11 |
| Prestw-1003 | 13E04 | Azapropazone | 0.91 | 1.21 |
| Prestw-1004 | 13E05 | Meptazinol hydrochloride | 0.93 | 1.17 |
| Prestw-1005 | 13E06 | Apramycin | 0.97 | 1.25 |
| Prestw-1006 | 13E07 | Epitiostanol | 0.97 | 1.18 |
| Prestw-1007 | 13E08 | Fursultiamine Hydrochloride | 0.90 | 1.22 |
| Prestw-1008 | 13E09 | Gabexate mesilate | 0.96 | 1.08 |
| Prestw-1009 | 13E10 | Pivampicillin | 1.01 | 1.17 |
| Code    | Category   | Name                                      | Min | Max |
|---------|------------|-------------------------------------------|-----|-----|
| Prestw-1010 | 13E11      | Talampicillin hydrochloride               | 0.87| 1.26|
| Prestw-1011 | 13F02      | Flucloxacillin sodium                    | 0.95| 1.16|
| Prestw-1012 | 13F03      | Trapidil                                 | 0.89| 1.13|
| Prestw-1013 | 13F04      | Deptropine citrate                       | 0.85| 0.95|
| Prestw-1014 | 13F05      | Sertraline                               | 0.97| 0.64|
| Prestw-1015 | 13F06      | Ethamsylate                              | 0.99| 1.28|
| Prestw-1016 | 13F07      | Moxonidine                               | 0.96| 1.28|
| Prestw-1017 | 13F08      | Etilefrine hydrochloride                 | 1.01| 1.21|
| Prestw-1018 | 13G02      | Alprostadil                              | 0.93| 0.86|
| Prestw-1019 | 13G03      | Tocainide hydrochloride                  | 0.94| 1.27|
| Prestw-1020 | 13F10      | Torsemide                                | 0.91| 1.24|
| Prestw-1021 | 13G04      | Halofantrine hydrochloride               | 0.90| 0.87|
| Prestw-1022 | 13G05      | Risperidone                              | 0.93| 1.05|
| Prestw-1023 | 13G06      | Benzathine benzylpenicillin              | 0.87| 1.28|
| Prestw-1024 | 13G07      | Arbutin                                  | 0.84| 1.21|
| Prestw-1025 | 13G08      | Tocainide hydrochloride                  | 0.94| 1.37|
| Prestw-1026 | 13G09      | Benzaldehyde                             | 0.87| 1.28|
| Prestw-1027 | 13G10      | Risperidone                              | 0.93| 1.05|
| Prestw-1028 | 13G11      | Torsemide                                | 0.91| 1.24|
| Prestw-1029 | 13H02      | Halofantrine hydrochloride               | 0.90| 0.87|
| Prestw-1030 | 13H03      | Articaine hydrochloride                  | 0.93| 0.82|
| Code     | Name                        | Code | Value1 | Value2 |
|----------|-----------------------------|------|--------|--------|
| Prestw-1033 | Nomegestrol acetate          | 13H04 | 0.91   | 0.87   |
| Prestw-1034 | Pancuronium bromide         | 13H05 | 0.89   | 0.91   |
| Prestw-1035 | Molindone hydrochloride     | 13H06 | 0.88   | 1.04   |
| Prestw-1036 | Alcuronium chloride         | 13H07 | 0.88   | 1.10   |
| Prestw-1037 | Zalcitabine                 | 13H08 | 0.93   | 1.24   |
| Prestw-1038 | Methyldopate hydrochloride  | 13H09 | 0.91   | 1.27   |
| Prestw-1039 | Levocabastine hydrochloride | 13H10 | 0.90   | 1.25   |
| Prestw-1040 | Pyrvinium pamoate           | 13H11 | 0.96   | 1.39   |
| Plate 14  | Etomidate                   | 14A02 | 1.04   | 0.90   |
| Prestw-1041 | Tridihexethyl chloride      | 14A03 | 1.01   | 0.86   |
| Prestw-1042 | Penbutolol sulfate          | 14A04 | 1.05   | 0.83   |
| Prestw-1043 | Prednicarbate               | 14A05 | 1.05   | 0.81   |
| Prestw-1044 | Sertaconazole nitrate       | 14A06 | 1.01   | 0.82   |
| Prestw-1045 | Repaglinide                 | 14A07 | 1.00   | 0.95   |
| Prestw-1046 | Piretanide                  | 14A08 | 0.97   | 0.94   |
| Prestw-1047 | Piperacetazidine            | 14A09 | 0.86   | 0.84   |
| Prestw-1048 | Oxyphenbutazone             | 14A10 | 0.91   | 1.00   |
| Prestw-1049 | Quinethazone                | 14A11 | 1.32   | 1.24   |
| Prestw-1050 | Moricizine hydrochloride    | 14B02 | 0.96   | 0.93   |
| Prestw-1051 | Iopanoic acid               | 14B03 | 1.00   | 0.76   |
| Prestw-1052 | Pivmecillinam hydrochloride | 14B04 | 0.97   | 0.87   |
| Prestw-1053 | Levopropoxyphene napsylate  | 14B05 | 0.92   | 0.90   |
| Code    | Compound                           | Value1 | Value2 |
|---------|------------------------------------|--------|--------|
| Prestw-1055  | Piperidolate hydrochloride          | 0.98   | 0.87   |
| Prestw-1056  | Trifluridine                        | 0.96   | 0.92   |
| Prestw-1057  | Oxprenolol hydrochloride            | 1.00   | 0.92   |
| Prestw-1058  | Ondansetron Hydrochloride           | 0.96   | 0.91   |
| Prestw-1059  | Propoxycaine hydrochloride          | 1.03   | 0.90   |
| Prestw-1060  | Oxaproxin                           | 0.95   | 0.94   |
| Prestw-1061  | Phensuximide                        | 1.02   | 0.84   |
| Prestw-1062  | Ioxaglic acid                       | 1.07   | 1.10   |
| Prestw-1063  | Naftifine hydrochloride             | 0.97   | 0.84   |
| Prestw-1064  | Meprylcaine hydrochloride           | 0.90   | 0.94   |
| Prestw-1065  | Milrinone                           | 0.97   | 0.99   |
| Prestw-1066  | Methantheline bromide               | 1.00   | 0.91   |
| Prestw-1067  | Ticarcillin sodium                  | 0.96   | 1.02   |
| Prestw-1068  | Thiethylperazine malate             | 1.05   | 0.57   |
| Prestw-1069  | Mesalamine                          | 1.00   | 1.00   |
| Prestw-1362  | Vorinostat                          | 1.04   | 1.00   |
| Prestw-1071  | Imidurea                            | 0.89   | 0.96   |
| Prestw-1072  | Lansoprazole                        | 0.94   | 0.90   |
| Prestw-1073  | Bethanechol chloride                | 0.97   | 0.86   |
| Prestw-1074  | Cyproterone acetate                 | 1.01   | 0.95   |
| Prestw-1075  | (R)-Propranolol hydrochloride       | 0.95   | 1.08   |
| Prestw-1076  | Ciprofibrate                        | 1.03   | 1.05   |
| Prestw-1420  | Formestane                          | 0.98   | 0.97   |
| Prestw-1078 | 14D09  | Benzylpenicillin sodium | 0.94 | 0.97 |
| Prestw-1079 | 14D10  | Chlorambucil            | 0.94 | 1.14 |
| Prestw-1080 | 14D11  | Methiazole              | 0.95 | 1.06 |
| Prestw-1081 | 14E02  | (S)-propranolol hydrochloride | 0.93 | 1.06 |
| Prestw-1082 | 14E03  | (-)-Eseroline fumarate salt | 0.94 | 1.02 |
| Prestw-1294 | 14E04  | Isosorbide mononitrate  | 0.94 | 1.03 |
| Prestw-1084 | 14E05  | Leucomisine             | 0.98 | 1.07 |
| Prestw-1493 | 14E06  | Topiramate              | 0.96 | 1.05 |
| Prestw-1086 | 14E07  | D-cycloserine           | 0.95 | 1.06 |
| Prestw-1087 | 14E08  | 2-Chloropyrazine        | 1.02 | 1.07 |
| Prestw-1088 | 14E09  | (+,-)-Syneprine         | 0.98 | 1.11 |
| Prestw-1089 | 14E10  | (S)-(−)-Cycloserine     | 1.00 | 1.03 |
| Prestw-1090 | 14E11  | Homosalate              | 0.94 | 1.13 |
| Prestw-1091 | 14F02  | Spaglumic acid          | 0.95 | 1.10 |
| Prestw-1092 | 14F03  | Ranolazine              | 0.93 | 1.06 |
| Prestw-1443 | 14F04  | Misoprostol             | 0.94 | 1.18 |
| Prestw-1094 | 14F05  | Sulfadoxine             | 0.95 | 1.01 |
| Prestw-1095 | 14F06  | Cyclopentolate hydrochloride | 0.97 | 1.10 |
| Prestw-1096 | 14F07  | Estriol                 | 0.94 | 1.10 |
| Prestw-1097 | 14F08  | (-)-Isoproterenol hydrochloride | 0.95 | 1.13 |
| Prestw-1339 | 14F09  | Sarafloxacin           | 0.99 | 1.13 |
| Prestw-1099 | 14F10  | Nialamide               | 1.01 | 1.09 |
| Prestw-1195 | 14F11  | Toltrazuril            | 0.96 | 1.02 |
| Prestw-1101 | 14G02 | Perindopril | 0.88 | 1.08 |
|---|---|---|---|---|
| Prestw-1102 | 14G03 | Fexofenadine HCl | 0.90 | 0.99 |
| Prestw-1202 | 14G04 | 4-aminosalicylic acid | 0.90 | 1.15 |
| Prestw-1104 | 14G05 | Clonixin Lysinate | 0.96 | 1.04 |
| Prestw-1105 | 14G06 | Verteporfin | 0.84 | 1.12 |
| Prestw-1106 | 14G07 | Meropenem | 0.95 | 0.92 |
| Prestw-1107 | 14G08 | Ramipril | 0.92 | 1.03 |
| Prestw-1108 | 14G09 | Mephenytoin | 0.94 | 0.96 |
| Prestw-1109 | 14G10 | Rifabutin | 0.89 | 0.84 |
| Prestw-1110 | 14G11 | Parbendazole | 0.89 | 1.09 |
| Prestw-1111 | 14H02 | Mecamylamine hydrochloride | 0.92 | 0.81 |
| Prestw-1112 | 14H03 | Procarbazine hydrochloride | 0.96 | 0.81 |
| Prestw-1113 | 14H04 | Viomycin sulfate | 0.87 | 0.85 |
| Prestw-1114 | 14H05 | Saquinavir mesylate | 0.92 | 0.78 |
| Prestw-1115 | 14H06 | Ronidazole | 0.96 | 0.99 |
| Prestw-1116 | 14H07 | Dorzolamide hydrochloride | 0.89 | 1.14 |
| Prestw-1117 | 14H08 | Azaperone | 0.96 | 1.22 |
| Prestw-1118 | 14H09 | Cefepime hydrochloride | 0.92 | 1.23 |
| Prestw-1119 | 14H10 | Clocortolone pivalate | 0.90 | 1.23 |
| Prestw-1120 | 14H11 | Nadifloxacin | 1.07 | 1.20 |
| Plate 15 | 15A02 | Buspirone hydrochloride | 1.07 | 0.90 |
| Prestw-1283 | 15A03 | Anastrozole | 1.36 | 1.09 |
| Code     | Name                                | 1   | 2  |
|----------|-------------------------------------|-----|----|
| Prestw-  | Doxycycline hydrochloride           | 1.30| 0.78|
| 1399     |                                    |     |    |
| Prestw-  | Sulbactam                           | 1.11| 0.85|
| 1345     |                                    |     |    |
| Prestw-  | Fleroxacin                          | 1.08| 0.87|
| 1414     |                                    |     |    |
| Prestw-  | Potassium clavulanate               | 1.04| 1.08|
| 1315     |                                    |     |    |
| Prestw-  | Valproic acid                       | 1.08| 1.16|
| 1482     |                                    |     |    |
| Prestw-  | Mepivacaine hydrochloride           | 1.06| 1.06|
| 1280     |                                    |     |    |
| Prestw-  | Rifaxim                             | 1.09| 1.06|
| 1478     |                                    |     |    |
| Prestw-  | Estradiol Valerate                  | 1.01| 1.16|
| 1473     |                                    |     |    |
| Prestw-  | Acetylcysteine                      | 1.03| 0.86|
| 1206     |                                    |     |    |
| Prestw-  | Melengestrol acetate                | 1.43| 0.80|
| 1435     |                                    |     |    |
| Prestw-  | Bromhexine hydrochloride            | 1.08| 0.73|
| 1246     |                                    |     |    |
| Prestw-  | Anethole-trithione                  | 1.03| 0.80|
| 1223     |                                    |     |    |
| Prestw-  | Amcinonide                          | 1.08| 0.72|
| 1476     |                                    |     |    |
| Prestw-  | Caffeine                            | 1.08| 0.76|
| 1256     |                                    |     |    |
| Prestw-  | Carvedilol                          | 1.17| 0.73|
| 1262     |                                    |     |    |
| Prestw-  | Methenamine                         | 1.06| 0.99|
| 1282     |                                    |     |    |
| Prestw-  | Phentermine hydrochloride           | 1.11| 0.98|
| 1308     |                                    |     |    |
| Prestw-  | Diclazuril                          | 1.12| 0.92|
| 1394     |                                    |     |    |
| Prestw-  | Famciclovir                         | 1.09| 0.84|
| 1249     |                                    |     |    |
| Prestw-  | Dopamine hydrochloride              | 1.06| 1.05|
| 1398     |                                    |     |    |
| Prestw-  | Cefdinir                            | 1.04| 0.78|
| 1263     |                                    |     |    |
| Prestw-  | Carprofen                           | 1.13| 0.91|
| 1261     |                                    |     |    |
| Prestw-  | Celecoxib                           | 1.06| 0.87|
| 1371     |                                    |     |    |
| Code     | Name                           | Value1 | Value2 |
|----------|--------------------------------|--------|--------|
| Prestw-1258 | 15C07 Candesartan            | 1.04   | 0.83   |
| Prestw-1483 | 15C08 Fludarabine              | 1.03   | 0.90   |
| Prestw-1484 | 15C09 Cladribine                | 0.98   | 1.12   |
| Prestw-1356 | 15C10 Vardenafil               | 1.07   | 1.00   |
| Prestw-1417 | 15C11 Fluconazole               | 0.98   | 0.84   |
| Prestw-1203 | 15D02 5-fluorouracil           | 1.01   | 0.95   |
| Prestw-1487 | 15D03 Mesna                    | 0.95   | 1.06   |
| Prestw-1444 | 15D04 Mitotane                 | 0.99   | 0.83   |
| Prestw-1497 | 15D05 Ambrisentan              | 0.93   | 0.95   |
| Prestw-1479 | 15D06 Triclosan                | 1.06   | 0.91   |
| Prestw-1401 | 15D07 Enoxacin                 | 1.06   | 0.89   |
| Prestw-1307 | 15D08 Olopatadine hydrochloride | 1.08   | 0.85   |
| Prestw-1187 | 15D09 Granisetron              | 1.03   | 1.00   |
| Prestw-1224 | 15D10 Anthralin                | 1.04   | 1.07   |
| Prestw-1492 | 15D11 Lamotrigine              | 0.99   | 0.76   |
| Prestw-1383 | 15E02 Clofibrate               | 0.93   | 1.09   |
| Prestw-1481 | 15E03 Cyclophosphamide         | 0.91   | 1.05   |
| Prestw-1229 | 15E04 Aripiprazole             | 1.03   | 1.01   |
| Prestw-1405 | 15E05 Ethinylestradiol        | 1.03   | 0.97   |
| Prestw-1419 | 15E06 Fluocinolone acetonide   | 0.93   | 0.90   |
| Prestw-1343 | 15E07 Sparfloxacin             | 0.95   | 0.90   |
| Prestw-1390 | 15E08 Desloratadine            | 0.98   | 0.51   |
| Prestw-1378 | 15E09 Clarithromycin           | 0.92   | 0.94   |
| Code     | Code2 | Name                              | Value1 | Value2 |
|---------|-------|-----------------------------------|--------|--------|
| Prestw-| 1199  | Tripelennamine hydrochloride      | 0.98   | 0.92   |
| Prestw-| 1352  | Tulobuterol                       | 1.05   | 1.00   |
| Prestw-| 1196  | Topotecan                         | 0.99   | 1.09   |
| Prestw-| 1232  | Atorvastatin                      | 1.01   | 1.03   |
| Prestw-| 1234  | Azithromycin                      | 0.96   | 0.98   |
| Prestw-| 1286  | Ibudilast                         | 0.92   | 0.94   |
| Prestw-| 1433  | Losartan                          | 0.87   | 0.93   |
| Prestw-| 1236  | Benztropine mesylate              | 0.91   | 0.61   |
| Prestw-| 1359  | Vecuronium bromide                | 1.00   | 0.88   |
| Prestw-| 1350  | Telmisartan                       | 1.05   | 1.02   |
| Prestw-| 1490  | Nalmefene hydrochloride           | 0.97   | 0.85   |
| Prestw-| 1241  | Bifonazole                        | 0.85   | 0.87   |
| Prestw-| 1265  | Gatifloxacin                      | 0.95   | 0.99   |
| Prestw-| 1265  | Bosentan                          | 1.07   | 0.93   |
| Prestw-| 1244  | Gemcitabine                       | 0.79   | 0.84   |
| Prestw-| 1266  | Olmesartan                        | 0.84   | 0.59   |
| Prestw-| 1190  | Racepinephrine HCl                | 0.91   | 0.94   |
| Prestw-| 1480  | Montelukast                       | 0.95   | 1.02   |
| Prestw-| 1189  | Docetaxel                         | 0.94   | 0.91   |
| Prestw-| 1180  | Cilnidipine                       | 0.96   | 0.97   |
| Prestw-| 1376  | Imiquimod                         | 0.97   | 1.00   |
| Prestw-| 1291  | Fosinopril                        | 0.87   | 0.97   |
| Prestw-| 1423  | Imatinib                          | 0.90   | 0.72   |
| Prestw-| 1290  |                                 |        |        |
| Code       | Code | Name                    | Value_1 | Value_2 |
|------------|------|-------------------------|---------|---------|
| Prestw-1446| 15H03| Moxifloxacin            | 0.89    | 0.70    |
| Prestw-1421| 15H04| Formoterol fumarate     | 0.91    | 0.65    |
| Prestw-1338| 15H05| Rufloxacin              | 0.94    | 0.77    |
| Prestw-1319| 15H06| Pravastatin             | 0.99    | 0.82    |
| Prestw-1337| 15H07| Rosiglitazone           | 0.90    | 0.98    |
| Prestw-1334| 15H08| Rivastigmine            | 0.90    | 0.98    |
| Prestw-1342| 15H09| Sildenafil               | 0.92    | 1.03    |
| Prestw-1207| 15H10| Acetylsalicylic acid    | 0.88    | 0.99    |
| Prestw-1472| 15H11| Hexachlorophene         | 0.95    | 0.99    |
Supplemental Table 2. Compounds of the Prestwick Chemical Library excluded from analysis. Compounds that had a fold-change ≥ 1.3 in the K562-NL alone condition were excluded from analysis as these drugs cytotoxic to K562-NL cells in absence of NK92 cells.

| Prestw number | Plate # / Well position | Chemical name                  | average fold-change |
|---------------|-------------------------|--------------------------------|---------------------|
| Prestw-349    | 05C10                   | Ritodrine hydrochloride        | 1.69                |
| Prestw-369    | 05E10                   | Meloxicam                      | 1.50                |
| Prestw-339    | 05B10                   | Guanfacine hydrochloride       | 1.44                |
| Prestw-925    | 12E06                   | Thonzonium bromide             | 1.36                |
| Prestw-143    | 02G04                   | Chlorhexidine                  | 1.36                |
| Prestw-1152   | 05F10                   | Nefazodone HCl                 | 1.34                |
| Prestw-1435   | 15B03                   | Melengestrol acetate           | 1.43                |
| Prestw-705    | 09G06                   | Methyl benzethonium chloride   | 1.32                |
| Prestw-1050   | 14A11                   | Quinethazone                   | 1.32                |
| Prestw-1399   | 15A04                   | Doxycycline hydrochloride      | 1.30                |
| Prestw-777    | 10F08                   | Alexidine dihydrochloride      | 16.01               |
| Prestw-1222   | 15A03                   | Anastrozole                    | 1.36                |
Supplemental Table 3. Z’ factor for individual assay plates from the screening of the Prestwick Chemical Library. Z’ factor was calculated using the positive and negative control luminescent values from each plate.

| Plate # | K562-NL alone | 1:1 E:T |
|---------|---------------|---------|
| 1       | 0.84          | 0.64    |
| 2       | 0.67          | 0.52    |
| 3       | 0.63          | 0.20    |
| 4       | 0.75          | 0.43    |
| 5       | 0.66          | 0.50    |
| 6       | 0.64          | 0.56    |
| 7       | 0.74          | 0.80    |
| 8       | 0.73          | 0.28    |
| 9       | 0.75          | 0.54    |
| 10      | 0.81          | 0.55    |
| 11      | 0.80          | 0.56    |
| 12      | 0.79          | 0.68    |
| 13      | 0.77          | 0.51    |
| 14      | 0.74          | -0.06   |
| 15      | 0.50          | 0.06    |
| Average | 0.72          | 0.44    |