

THOMSON REUTERS INTEGRITY

QUICK GUIDE SERIES: No. 11



DRUG RE-PROFILING USING THOMSON REUTERS INTEGRITY

Does your company have technology that could support repurposing of known drugs, including those that didn't make it to the market because they weren't efficacious enough?

Find out how *Thomson Reuters Integrity*SM can help your drug re-profiling research by pinpointing potential products of interest. Benefit from intuitive filtering tools within *Integrity* to narrow down your research results and identify products that may be suitable for re-profiling.

You can also use *Integrity* to gather All Related Information associated with your potential product in different Knowledge Areas to try to understand why development hasn't advanced and what recent activity there has been around the drug.

This step-by-step guide will show you how to:

- Search for drugs with low solubility
- Filter by Statistics to narrow down your results
- Create a data trends view of your results
- Find compounds of potential interest for your technology

EXAMPLE SCENARIO: DRUG RE-PROFILING USING THOMSON REUTERS INTEGRITY

A company has a new platform technology to improve solubility of orally administered compounds. Their biochemists would like to search *Integrity* for known drugs developed for HIV infection that did not make it to the market because of inefficacy due to low solubility.

1. SEARCH FOR DRUGS WITH PHARMACOKINETIC VALUES INDICATING POTENTIAL SOLUBILITY ISSUES

- To search for compounds with specific pharmacokinetic values for a certain parameter you should start with a search in the **Pharmacokinetics/Metabolism Knowledge Area**. In the **advanced search** form you can select Administered Product and then the Administration Route field; in this case we are interested in the solubility of orally administered compounds. (FIGURE 1)
- Using the **new search field called Value**, in the **Measured Product** submenu, you can search for low PK values for a particular parameter. For a surrogate measure of solubility select bioavailability (F), which is often limited by low solubility, and add units, in this case percentage, and define the **values** you wish to find, in this example less than 50 percent. (FIGURE 2)
- Anti-HIV Agents can be added using **Therapeutic Group** in the product section. Finally, to find products that never made it to market, use the **Highest Phase** field in the product section and include all phases up to phase III.

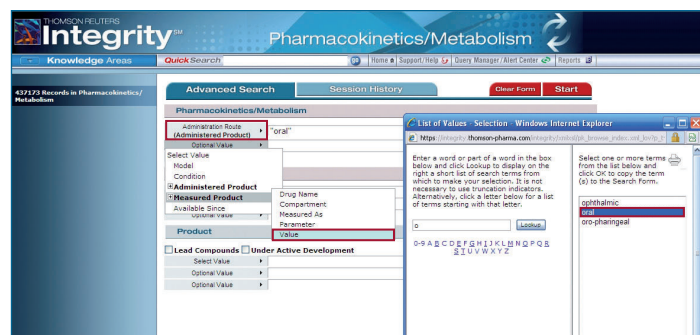


FIGURE 1

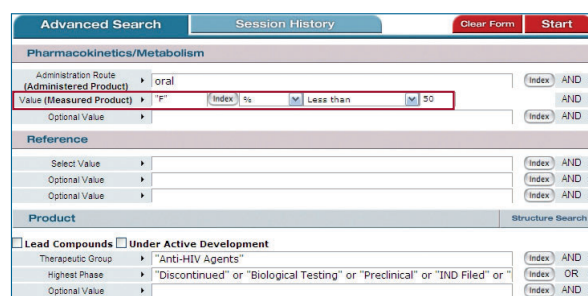


FIGURE 2

Records Retrieved: 234 in Pharmacokinetics/ Metabolism

Pharmacokinetics/Metabolism Search Results

Query > Administration Route = oral AND Value = LESS THAN 50 AND Parameter = "F" AND Unit = % AND Therapeutic Group = "Anti-HIV Agents" AND Highest Phase = "Discontinued" or "Biological Testing" or "Preclinical" or "IND Filed" or "Phase I" or "Phase II" or "Phase III" or "Phase IV"

Administered Product	Measured Product	Biomarker	Model	Condition	Source
<input type="checkbox"/> (+)-Dihydrocalanolid A 50 · 10 ⁻³ g/kg p.o. s.d.	(+)-Dihydrocalanolid A F 46.8 % HPLC		Mice Male		Ref. 1
<input type="checkbox"/> (283324) 0.1 g/kg p.o. s.d.	283324 F 42 % HPLC		Mice Female		Ref. 2
<input type="checkbox"/> (283324) 0.1 g/kg p.o. s.d.	283324 F 25 % HPLC		Rats Female		Ref. 2
<input type="checkbox"/> (241797) 10 · 10 ⁻³ g/kg p.o. s.d.	241797 F Plasma 27 %		Dogs		Ref. 3
<input type="checkbox"/> (245124) 10 · 10 ⁻³ g/kg p.o. s.d.	245124 F 41.1 %		Rats		Ref. 4
<input type="checkbox"/> (265470) 10 · 10 ⁻³ g/kg p.o. s.d.	265470 F 29 %		Dogs		Ref. 5

FIGURE 3

Tip:

- To find a list of parameter abbreviations and definitions, click **Frequently Asked Questions** either on the bottom left-hand side of the *Integrity* homepage or under the Support/Help tab on the navigation bar.
- Use the **Browse Indexes** (Index button to the right of the search field) to select and copy search terms to the form.
- Click **Start** to launch your search and display results. (FIGURE 3)
- To view the associated references, click the **reference link** in the source column on the right. In the popup window you will find the reference information and links to *PubMed*[®] and *Web of Knowledge*SM where available. (FIGURE 4)



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- Now use the **Filter by Statistics** function to the right of the results list to narrow down your results. For example, click to select the **Model**. From the chart use the checkboxes to select all human models and then click **View Subset(s)** to display these. (FIGURE 5)
- To view bioavailability data trends you can select the **Calculate Mean/Median Values** option from the **Options** pull-down menu. (FIGURE 6)
- In this example, click the radio button next to Mean to calculate mean values.
- Mean values are displayed for each administered product in the original results list. (FIGURE 7)
- Close the Mean values pop-up to return to the pharmacokinetics results list.

FIGURE 4

FIGURE 5

2. FIND COMPOUNDS OF POTENTIAL INTEREST FOR YOUR RESEARCH

- To review further information from other Knowledge Areas that is associated with these results, you can open the **Options** pull-down menu and click **All Related Information via Quick Search**. The display will then allow you to view the information related to your PK data in the other areas. (FIGURE 8)
- To review the drug records to pinpoint potential products suitable for reprofiling, click the **Drugs & Biologics** link.
- To see the full product records open the **Options** pull-down menu and select **Full Records**.
- Once you have identified an interesting product, you can get background information before contacting the company to offer your technology. For example, look at the **Experimental Pharmacology** data to see the activity levels and at the **Literature** references to try to understand why development hasn't advanced and what recent activity there has been around the drug. (FIGURE 9)

Administered Product & Dose	Model	F (%)
Adefovir (Solution) 3*10 ³ g/kg p.o. s.d. Humans: Adult	22	52 (n=1)
Beverimat (Capsules (controlled-release)) 25*10 ³ p.p.o. s.d. Humans: Adult	28	28 (n=1)
Beverimat (Capsules (entero-coated)) 25*10 ³ p.p.o. s.d. Humans: Adult, Fasted	28	28 (n=1)
Didanosine (Solution) 0.1 g.p.o. s.d. Humans: Male, Adult, Fasted	33.6	

FIGURE 7

FIGURE 8

Chemical Structure
C[C@H]1[C@@H](OC(=O)C2=CC=CC=C2)[C@H](OC(=O)C3=CC=CC=C3)[C@@H](OC(=O)C4=CC=CC=C4)[C@H](OC(=O)C5=CC=CC=C5)[C@H](OC(=O)C6=CC=CC=C6)[C@H](OC(=O)C7=CC=CC=C7)[C@H](OC(=O)C8=CC=CC=C8)[C@H](OC(=O)C9=CC=CC=C9)[C@H](OC(=O)C10=CC=CC=C10)[C@H](OC(=O)C11=CC=CC=C11)[C@H](OC(=O)C12=CC=CC=C12)[C@H](OC(=O)C13=CC=CC=C13)[C@H](OC(=O)C14=CC=CC=C14)[C@H](OC(=O)C15=CC=CC=C15)[C@H](OC(=O)C16=CC=CC=C16)[C@H](OC(=O)C17=CC=CC=C17)[C@H](OC(=O)C18=CC=CC=C18)[C@H](OC(=O)C19=CC=CC=C19)[C@H](OC(=O)C20=CC=CC=C20)[C@H](OC(=O)C21=CC=CC=C21)[C@H](OC(=O)C22=CC=CC=C22)[C@H](OC(=O)C23=CC=CC=C23)[C@H](OC(=O)C24=CC=CC=C24)[C@H](OC(=O)C25=CC=CC=C25)[C@H](OC(=O)C26=CC=CC=C26)[C@H](OC(=O)C27=CC=CC=C27)[C@H](OC(=O)C28=CC=CC=C28)[C@H](OC(=O)C29=CC=CC=C29)[C@H](OC(=O)C30=CC=CC=C30)[C@H](OC(=O)C31=CC=CC=C31)[C@H](OC(=O)C32=CC=CC=C32)[C@H](OC(=O)C33=CC=CC=C33)[C@H](OC(=O)C34=CC=CC=C34)[C@H](OC(=O)C35=CC=CC=C35)[C@H](OC(=O)C36=CC=CC=C36)[C@H](OC(=O)C37=CC=CC=C37)[C@H](OC(=O)C38=CC=CC=C38)[C@H](OC(=O)C39=CC=CC=C39)[C@H](OC(=O)C40=CC=CC=C40)[C@H](OC(=O)C41=CC=CC=C41)[C@H](OC(=O)C42=CC=CC=C42)[C@H](OC(=O)C43=CC=CC=C43)[C@H](OC(=O)C44=CC=CC=C44)[C@H](OC(=O)C45=CC=CC=C45)[C@H](OC(=O)C46=CC=CC=C46)[C@H](OC(=O)C47=CC=CC=C47)[C@H](OC(=O)C48=CC=CC=C48)[C@H](OC(=O)C49=CC=CC=C49)[C@H](OC(=O)C50=CC=CC=C50)[C@H](OC(=O)C51=CC=CC=C51)[C@H](OC(=O)C52=CC=CC=C52)[C@H](OC(=O)C53=CC=CC=C53)[C@H](OC(=O)C54=CC=CC=C54)[C@H](OC(=O)C55=CC=CC=C55)[C@H](OC(=O)C56=CC=CC=C56)[C@H](OC(=O)C57=CC=CC=C57)[C@H](OC(=O)C58=CC=CC=C58)[C@H](OC(=O)C59=CC=CC=C59)[C@H](OC(=O)C60=CC=CC=C60)[C@H](OC(=O)C61=CC=CC=C61)[C@H](OC(=O)C62=CC=CC=C62)[C@H](OC(=O)C63=CC=CC=C63)[C@H](OC(=O)C64=CC=CC=C64)[C@H](OC(=O)C65=CC=CC=C65)[C@H](OC(=O)C66=CC=CC=C66)[C@H](OC(=O)C67=CC=CC=C67)[C@H](OC(=O)C68=CC=CC=C68)[C@H](OC(=O)C69=CC=CC=C69)[C@H](OC(=O)C70=CC=CC=C70)[C@H](OC(=O)C71=CC=CC=C71)[C@H](OC(=O)C72=CC=CC=C72)[C@H](OC(=O)C73=CC=CC=C73)[C@H](OC(=O)C74=CC=CC=C74)[C@H](OC(=O)C75=CC=CC=C75)[C@H](OC(=O)C76=CC=CC=C76)[C@H](OC(=O)C77=CC=CC=C77)[C@H](OC(=O)C78=CC=CC=C78)[C@H](OC(=O)C79=CC=CC=C79)[C@H](OC(=O)C80=CC=CC=C80)[C@H](OC(=O)C81=CC=CC=C81)[C@H](OC(=O)C82=CC=CC=C82)[C@H](OC(=O)C83=CC=CC=C83)[C@H](OC(=O)C84=CC=CC=C84)[C@H](OC(=O)C85=CC=CC=C85)[C@H](OC(=O)C86=CC=CC=C86)[C@H](OC(=O)C87=CC=CC=C87)[C@H](OC(=O)C88=CC=CC=C88)[C@H](OC(=O)C89=CC=CC=C89)[C@H](OC(=O)C90=CC=CC=C90)[C@H](OC(=O)C91=CC=CC=C91)[C@H](OC(=O)C92=CC=CC=C92)[C@H](OC(=O)C93=CC=CC=C93)[C@H](OC(=O)C94=CC=CC=C94)[C@H](OC(=O)C95=CC=CC=C95)[C@H](OC(=O)C96=CC=CC=C96)[C@H](OC(=O)C97=CC=CC=C97)[C@H](OC(=O)C98=CC=CC=C98)[C@H](OC(=O)C99=CC=CC=C99)[C@H](OC(=O)C100=CC=CC=C100)[C@H](OC(=O)C101=CC=CC=C101)[C@H](OC(=O)C102=CC=CC=C102)[C@H](OC(=O)C103=CC=CC=C103)[C@H](OC(=O)C104=CC=CC=C104)[C@H](OC(=O)C105=CC=CC=C105)[C@H](OC(=O)C106=CC=CC=C106)[C@H](OC(=O)C107=CC=CC=C107)[C@H](OC(=O)C108=CC=CC=C108)[C@H](OC(=O)C109=CC=CC=C109)[C@H](OC(=O)C110=CC=CC=C110)[C@H](OC(=O)C111=CC=CC=C111)[C@H](OC(=O)C112=CC=CC=C112)[C@H](OC(=O)C113=CC=CC=C113)[C@H](OC(=O)C114=CC=CC=C114)[C@H](OC(=O)C115=CC=CC=C115)[C@H](OC(=O)C116=CC=CC=C116)[C@H](OC(=O)C117=CC=CC=C117)[C@H](OC(=O)C118=CC=CC=C118)[C@H](OC(=O)C119=CC=CC=C119)[C@H](OC(=O)C120=CC=CC=C120)[C@H](OC(=O)C121=CC=CC=C121)[C@H](OC(=O)C122=CC=CC=C122)[C@H](OC(=O)C123=CC=CC=C123)[C@H](OC(=O)C124=CC=CC=C124)[C@H](OC(=O)C125=CC=CC=C125)[C@H](OC(=O)C126=CC=CC=C126)[C@H](OC(=O)C127=CC=CC=C127)[C@H](OC(=O)C128=CC=CC=C128)[C@H](OC(=O)C129=CC=CC=C129)[C@H](OC(=O)C130=CC=CC=C130)[C@H](OC(=O)C131=CC=CC=C131)[C@H](OC(=O)C132=CC=CC=C132)[C@H](OC(=O)C133=CC=CC=C133)[C@H](OC(=O)C134=CC=CC=C134)[C@H](OC(=O)C135=CC=CC=C135)[C@H](OC(=O)C136=CC=CC=C136)[C@H](OC(=O)C137=CC=CC=C137)[C@H](OC(=O)C138=CC=CC=C138)[C@H](OC(=O)C139=CC=CC=C139)[C@H](OC(=O)C140=CC=CC=C140)[C@H](OC(=O)C141=CC=CC=C141)[C@H](OC(=O)C142=CC=CC=C142)[C@H](OC(=O)C143=CC=CC=C143)[C@H](OC(=O)C144=CC=CC=C144)[C@H](OC(=O)C145=CC=CC=C145)[C@H](OC(=O)C146=CC=CC=C146)[C@H](OC(=O)C147=CC=CC=C147)[C@H](OC(=O)C148=CC=CC=C148)[C@H](OC(=O)C149=CC=CC=C149)[C@H](OC(=O)C150=CC=CC=C150)[C@H](OC(=O)C151=CC=CC=C151)[C@H](OC(=O)C152=CC=CC=C152)[C@H](OC(=O)C153=CC=CC=C153)[C@H](OC(=O)C154=CC=CC=C154)[C@H](OC(=O)C155=CC=CC=C155)[C@H](OC(=O)C156=CC=CC=C156)[C@H](OC(=O)C157=CC=CC=C157)[C@H](OC(=O)C158=CC=CC=C158)[C@H](OC(=O)C159=CC=CC=C159)[C@H](OC(=O)C160=CC=CC=C160)[C@H](OC(=O)C161=CC=CC=C161)[C@H](OC(=O)C162=CC=CC=C162)[C@H](OC(=O)C163=CC=CC=C163)[C@H](OC(=O)C164=CC=CC=C164)[C@H](OC(=O)C165=CC=CC=C165)[C@H](OC(=O)C166=CC=CC=C166)[C@H](OC(=O)C167=CC=CC=C167)[C@H](OC(=O)C168=CC=CC=C168)[C@H](OC(=O)C169=CC=CC=C169)[C@H](OC(=O)C170=CC=CC=C170)[C@H](OC(=O)C171=CC=CC=C171)[C@H](OC(=O)C172=CC=CC=C172)[C@H](OC(=O)C173=CC=CC=C173)[C@H](OC(=O)C174=CC=CC=C174)[C@H](OC(=O)C175=CC=CC=C175)[C@H](OC(=O)C176=CC=CC=C176)[C@H](OC(=O)C177=CC=CC=C177)[C@H](OC(=O)C178=CC=CC=C178)[C@H](OC(=O)C179=CC=CC=C179)[C@H](OC(=O)C180=CC=CC=C180)[C@H](OC(=O)C181=CC=CC=C181)[C@H](OC(=O)C182=CC=CC=C182)[C@H](OC(=O)C183=CC=CC=C183)[C@H](OC(=O)C184=CC=CC=C184)[C@H](OC(=O)C185=CC=CC=C185)[C@H](OC(=O)C186=CC=CC=C186)[C@H](OC(=O)C187=CC=CC=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